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ROENTGENOLOGIC MANIFESTATIONS OF GIANT-CELL TUMOR*

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SINCE the publication, in 1860, of Nélaton's first monograph on giant-cell tumors, the subject has been widely discussed. This is attested by more than 100 articles in which these tumors are considered or reports of cases are given, and perhaps twice that number concerning bone tumors in which the giant-cell type is mentioned, described, or distinguished from other varieties. Possibly the reason for this vast amount of literature is the rarity of giant-cell tumors and the small number seen by the individual physician. Codman stated that the average pathologist will not see more than ten osteogenic sarcomas in his whole experience. At The Mayo Clinic the proportion of giant-cell tumors to osteogenic sarcomas has been less than one to five, and if this ratio holds generally, and Codman's estimate is correct, the allotment for the average practitioner would be one or two cases, if indeed any.

Nélaton vividly pointed out that giant-cell tumors are not malignant sarcomas, but, as in many other conditions discovered long ago, little of real value has been added to knowledge of the disease, save that roentgenography has become a valuable aid in diagnosis, and authorities such as Bloodgood, Barrie, Coley, Ewing, Kolodny and Meyerding have greatly popularized among the general profession the idea that giant-cell tumors are benign.

The advent of the roentgen ray markedly stimulated the study of pathologic changes in bone, but prior to 1910 roentgenologic distinction between giant-cell tumor and osteogenic sarcoma was not possible. As late as 1920 many extremities were needlessly sacrificed by good surgeons because of an incorrect diagnosis, and errors in the roentgenologic diagnosis continue to occur with considerable frequency. A desire to determine the causes of such errors led us to study 110 cases of giant-cell tumor observed at The Mayo Clinic from 1909 to 1929 inclusive. Of these, the diagnosis was proved by operation or biopsy in 86 cases; in 24 cases neither operation nor biopsy was performed, but the clinical and roentgenologic data were deemed adequate to sustain the diagnosis. Outstanding among the impressions gained from our review of this series is the conviction that, contrary

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to accepted belief, the roentgenologic picture of giant-cell tumor is not single but dual.

Ordinarily when the roentgenologist thinks of giant-cell tumor, he visualizes a

FIG. 1. Common type of giant-cell tumor with many trabeculae, in lower end of radius.

central bone tumor, usually in the head of a long bone, expanding the cortex but not breaking through it, and traversed by trabeculae dividing the tumor into several, or numerously multiple, loculi. This variety is the one that has been almost universally described in the past and is easily recognized (Figs. 1 and 2). Two other bone tumors which might be confounded with it are enchondroma and bone cyst. However, both these lesions tend to expand the bone cylindrically, whereas giant-cell tumor expands abruptly from adjacent normal bone. Bone cysts are seldom trabeculated, and enchondromas occur most often in the bones of the hand. Since the cortex is wholly, or at least largely, intact, this type of giant-cell tumor scarcely will be mistaken for a malignant new growth. Even if the cortex of the bone has been penetrated and the soft tissues have been invaded, the lesion is not necessarily identified as bone sarcoma, or as a giant-cell tumor that has become malignant. In a recent article, Geschickter and Copeland, after they had reviewed the literature and had recounted studies of the largest series of cases yet reported, concluded that giant-cell tumor never develops into malignant osteogenic sarcoma. Irrespective of this contention, it is to be granted that a transradiant, trabeculated area in the end of a long bone, surrounded by a thinned and expanded, but unbroken cortex, is fairly diagnostic of giant-cell tumor. However, the fact is outstanding that this classic appearance was present in only half, approximately, of the cases in our series.

In the other half of the series, the manifestations were different. The roentgenograms gave evidence of homogeneous lysis of the central portion of the bone, the lysis extending toward the cortex, leaving only a thin shell of bone in some cases; in other cases the cortex was intact in only part of its circumference, and in still others the walls of the bone had been completely crushed out and the shaft had telescoped through or into the tumor (Figs. 3 and 4). The tumor was of about the same density

FIG. 2. Typical trabeculated giant-cell tumor in lower end of femur.

to radiation as other soft tissue, and the roentgenograms gave evidence of a hazy, homogeneous mass filling the space occupied by the dissolved bone, frequently extending out considerably beyond the cor-

tical surface and pushing the soft tissues ahead of it (Fig. 3). There was never any separation of the periosteum from the normal cortex beyond the uninvolved bone,

Fig. 3. Lysis type of giant-cell tumor with protrusion into soft tissues.

so often seen in osteogenic sarcomas, and called by Codman the reactive triangle. Little, if any, bony structure was visible in the tumor, the edges of the adjacent healthy bone were rather even and smooth, and there was no extension into the medullary cavity. The epiphyseal line did not act as a barrier, but the cartilage of the joint was seldom broken through except by trauma or in very advanced cases. This appearance was best demonstrated in tumors which occurred in the ends of the largest long bones of the skeleton, the femurs and tibias. This type of giant-cell tumor was most likely to occur where there was considerable spongy bone, such as the lower end of the femur, the vertebrae, the tarsal bones and the sacrum.

The gross pathologic changes in the second variety of tumor were about what would be suspected from the roentgenograms. The tumor space was filled with a fluid, gelatinous mass of soft consistence, that ran out when the tumor was incised. There might be a few large, cystic loculi, divided with thin laminae of bone, or spicules running out from the cortex. Often there was no formation whatever. Many of the old pathologic specimens, saved from the time when amputation was the usual treatment, were sawed lengthwise and studied. In most cases the fluid mass had been coagulated and hardened by the fixing fluid and was of about the consistence of very soft cheese. There was no fibrous or cartilaginous tissue in the tumor. In some of the cases the content had broken through the surrounding structures and had filled the joint space. Roentgenograms were made of all specimens removed by amputation, or of the parts of the involved bone removed grossly, and the films could be classified in the two varieties described. The tumors consisting of the small, multilocular spaces made excellent roentgenograms, whereas those of the homogeneous

Fig. 4. Lysis type of giant-cell tumor resembling sarcoma or metastasis.

variety produced indefinite shadows of soft tissue suddenly blending with the normal, adjacent bone. Roentgenograms of the second type bore a strong resemblance to

those of a single, large metastatic growth of the osteoblastic type, melting away the bone.

The relationship of these two varieties could only be surmised. The pathologic changes seen microscopically were the same in both, and the difference was only in the gross structure. The second variety was probably only an older, more advanced, or more active process of the same condition. Most tumors of the first kind were smaller than those of the second, and they progressed much more slowly. Some exhibited cystic trabeculation in the beginning, and later roentgenograms gave evidence of dissolution of the formation. In some cases the two varieties were shown in two different parts of the tumor. One side would be of homogeneous density, and the other side would have a reticular framework supporting the remaining bony capsule. Evidently the tumor tended to break down the small, bony partitions, and to form a conglomerate mass.

Regardless of the etiology of the two conditions, not all giant-cell tumors were characterized by the expansile, trabeculated bone tumor that the literature has emphasized. It is difficult to surmise what the roentgenologic appearance of each individual tumor may have been when it first produced symptoms. It is possible that all giant-cell tumors have their beginning as a trabeculated, multilocular tumor, and, due to extraneous conditions, change into the larger, homogeneous variety.

As in most diseases, the diagnosis of this tumor is best made by considering all available data. A roentgenogram in which is displayed evidence of the trabeculated, cystic tumor described is pathognomonic of the condition, and the roentgenologist seldom will err in making a positive diagnosis when he sees this, but in the other group the diagnosis may be in doubt until after operation and biopsy. Probably a good roentgenogram is the best single factor in arriving at a diagnosis, so much so that it is sometimes impossible to convince the roentgenologist, even after biopsy has been obtained and operation performed, that the lesion was not a giant-cell tumor. In other cases the roentgenologist will be inclined, when judging from the roentgenogram alone, to make a diagnosis of some other bone-destroying tumor, rather than of a giant-cell tumor, considering the latter as only a second or a third possibility. The quality of the roentgenogram, as well as the experience of the roentgenologist, is significant. Bone detail, and views in several directions, are of more value than stereoroentgenograms, because of the small size of the average tumor.

TABLE I

SITUATION OF 84 TUMORS

Upper end of humerus	3
Shaft of humerus	2
Lower end of humerus	1
Lower end of radius	5
Lower end of ulna	4
Upper end of femur	4
Lower end of femur	20
Upper end of tibia	10
Lower end of tibia	1
Upper end of fibula	3
Maxilla	9
Mandible	7
Ilium	4
Sacrum	2
Vertebra	2
Phalanx	2
Pubis	2
Malar bone	1
Rib	1
Cuboid bone	1

In the tabulation are shown the number and situation of the tumors in the sixteen different bones involved in 84 of our proved cases. The 20 cases in which there were multiple tumors are not included, for they will be considered later. The ends of the long bones were by far the most usual situation for these tumors. The femur alone claimed practically 28 per cent of our proved cases, and the extremities of the tibia were involved in practically 13 per cent. Approximately 38 per cent of all the tumors in our series of proved cases occurred about the knee joint. Several occurred in rare situations, such as the vertebrae, ribs and tarsal bones. Another rare

situation is the middle portion of the shafts of long bones; the 2 in our series were both in the shaft of the humerus. This rarity previously has been reported by one of us.[7] The age incidence in our series was about the same as others have found, varying from the youngest patient, six years, to the oldest, sixty. The largest number of tumors occurred in early adult life; more than half occurred between the ages of ten and thirty years. Three occurred in children aged less than ten years; 20 occurred in the second decade of life; 24 in the third decade; 19 in the fourth decade; 14 in the fifth decade, and only 5 occurred in the sixth decade. Fifty of the patients were females; 38 were males.

The duration of symptoms was rather difficult to ascertain. Twenty-seven patients had had symptoms for six months or less when they appeared at the Clinic for diagnosis and treatment. Twenty-three had had trouble for more than six months but less than twelve; 15 had complained for from one to two years. Several patients stated

Fig. 5. Giant-cell tumor in lower end of femur (see Fig. 6).

that the first symptom was a fracture following a slight injury, and the roentgenogram revealed a bone tumor with pathologic fracture; a few had had recurrent symptoms varying from a few to many years. In some cases the giant-cell tumor had been present for many years, with recurrences and inadequate treatment. In

Fig. 6. Extension of disease after seven months (see Fig. 5).

some of these, roentgenograms had been made at different times over a period of years, and the progress of the lesion could be closely followed (Figs. 5 and 6). In 2 of the 86 cases lesions were multiple in different bones. In one case the presence of an atypical form of multiple myeloma was considered, but the largest lesion, which was in the head of the fibula, was characteristic of the expansile, cystic type of giant-cell tumor. The lesion was operated on, biopsy was done, and a typical giant-cell tumor was discovered. The patient is still living and is enjoying fairly good health. In the other case, in which there were multiple, cystic, trabeculated regions in several bones, the roentgenograms suggested fibrocystic disease, except the lesion in the head of the fibula, which was typical of a giant-cell tumor. Biopsy revealed a foreign-body giant-cell tumor. Unfortunately, biopsy was not performed on any other bones in either case. The question arises: Is giant-cell tumor of bone a neoplastic or an inflammatory disease? Argu-

ments for both conceptions may be found in the literature.

Most of the patients in this series are living and well, some of them several years after diagnosis and treatment. We were unable to find a single case in which metastasis or malignant degeneration had developed.

SUMMARY

In a series of 86 proved cases of giant-cell tumor two roentgenologic types of the growth have been encountered with approximately equal frequency.

The first variety has been accurately described by many observers. It is a central tumor, situated most often in the end of a long bone, and it exhibits trabeculae and expands the cortex but does not break through it. Other tumors of bone which may be confounded with this type of giant-cell tumor are enchondromas and cysts of bone.

In the second type of giant-cell tumor, as we have observed it, trabeculation is conspicuously absent. The roentgenograms give evidence of homogeneous lysis of the affected area; the cortex is not only expanded but is dissolved wholly or in part, and the tumor projects into the soft tissues. In many cases, the irregularly destroyed cortex has the appearance of a thin layer of melting ice. This variety of giant-cell tumor might be mistaken for primary sarcoma or a massive metastatic growth.

Giant-cell tumor is not necessarily confined to the end of a long bone; exceptionally it may occur elsewhere in the shaft. Besides the long bones, the bones of the face, the vertebrae, the ribs and the tarsal bones are subject to the disease.

In this series, outstanding differences from other series reported were not observed in respect to age and sex of the patients or duration of the disease.*

* For discussion see page 188.

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THE TREATMENT OF GIANT-CELL BONE TUMORS BY ROENTGEN IRRADIATION*

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THE treatment of giant-cell tumors of bone by means of the roentgen ray covers a period of at least twenty-five years. So far as we know, one of us (Pfahler) was the first to treat such a case. Treatment was begun in this case in March, 1906, reported in 1907, and is reviewed now—Case I. In this paper, we are reviewing 26 cases from Dr. Pfahler's private and hospital clinics which have been treated between 1906 and 1931, and therefore cover a period of twenty-five years.

The diagnosis and the treatment of giant-cell tumors of bones have always been of unusual interest. Both phases have received much detailed study, and it is unfortunate that time will not permit a review of the excellent work done by many authors. We must, however, refer especially to the very helpful contributions in diagnosis by Ewing, Codman, Baetjer, Bloodgood, and Geschickter; and to the masterful work in both diagnosis and treatment of these tumors by Kienböck, Holzknecht, Herendeen, Borak, Groover and Christie, and Evans and Leucutia.

DIAGNOSIS

The diagnosis of any bone tumor is the primary requisite before beginning treatment, but time will not permit more than a brief discussion limited to the roentgen appearance, which fortunately is usually sufficient. The site of these tumors is generally in the ends of the long bones—most frequently the distal end of the femur, the proximal ends of the tibia and fibula, the distal end of the radius, the proximal end of the humerus, the outer end of the clavicle, and in the inferior maxilla. They are found with the greatest frequency during adolescence and early adult life, but may be present during childhood or old age. The roentgenogram reveals a symmetrical dilatation of the medullary cavity, divided by many septa, with a progressive thinning and expansion of the cortex, but always sharply defined, and not presenting an invasive appearance. (An appearance of invasion and malignancy in these cases is sometimes due to the projection of the diseased area over healthy bone, but this can be corrected by further roentgenographic study—Case III.) The general appearances are those of a multilocular cyst.

As a rule, the tumor remains limited by a thin capsule of bone which is laid down in advance of the tumor as a result of the tension placed on the periosteum. A fracture can easily occur, and if the tumor remains untreated it usually breaks through into the soft tissue or into the joint.

Incision of the tumor discloses a cheese-like or a currant-jelly-like substance, which when examined microscopically shows in greater part the characteristic giant cells which gives these tumors their name. As a rule, the tumor remains benign, localized, and does not give rise to metastases, but Stone and Ewing have reported a case which became malignant, and we presented before this Society a year ago in our series of osteogenic sarcomata a case (Case III) which had the appearances of a giant-cell bone tumor but which gave rise to metastases and ended fatally.

TREATMENT

The treatment formerly was surgical, and we were called upon to treat only recurrent tumors, or those patients who refused to take the surgeon's advice. The early cases were erroneously diagnosed as sarcoma both clinically and microscopically. The results which we obtained were

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so convincing that we have been called upon more and more to treat primary cases, and at present our associated surgeons rarely operate upon these tumors. Herendeen has estimated that 25 per cent have recurrences after operation. We think that without associated irradiation the percentage must be higher. A biopsy is necessary only when the diagnosis remains doubtful after a thorough roentgen examination by an experienced roentgenologist. When a biopsy is not done the roentgen examination must be most thorough and satisfactory. When an expert roentgenologist is in doubt, the pathologist is often also in doubt, as was shown in our previous paper.[1]

The objections to an operation or biopsy are the following:

1. Breaking down the defense mechanism—rupture of the capsule, if one is present.

2. Release of the tumor cells into normal tissue if there is any tendency toward malignant disease. This can be safeguarded by suitable preliminary irradiation.

3. If irradiation is contemplated, it often leads to delay, and the response to irradiation is retarded after incision or curettement. This has also been observed by Herendeen.

4. The possibility of infection is very great. Often these tumors are near the joint, and any infection may lead to serious joint complications.

We have had several cases in which operation was followed by a serious and troublesome osteomyelitis. After preliminary irradiation, a biopsy may be done, but this should be with as little traumatism as possible. The needle technique developed by Martin and Ellis seems to be successful and involves a minimum of traumatism.

The roentgen rays have been used by us in the treatment of giant-cell tumors of bone for twenty-five years. Formerly some of the cases recorded as sarcomas of bone, by others as well as one of us (G.E.P.), and in which good results were obtained, were really giant-cell tumors. We have had no case in which we failed to obtain definite improvement. The evidence of repair is shown by a deposit of lime along the cortex, on the inside. In general, the younger the child, the more rapid the healing of the bone. This rapid improvement in the young is most likely due to the more efficient repair mechanism which one finds in young bone. This rapid repair has also been observed we believe by all roentgenologists in fractures in young children as compared with old persons. In a comparative sense, the repair is slow in the older bones, especially if the tumor has developed slowly. In our experience, when the patient is young and otherwise healthy, there is definite evidence of repair within a month, while in old persons there may be no demonstrable evidence of bone deposit for two or three months. This observation has also been made by Herendeen, Holfelder, and Borak.

TECHNIQUE

In the early cases we used low voltage roentgen rays with only sole leather, or 1 to 6 mm. of aluminum as filters, and in the young, in whom we had to deal with relatively small bones, we obtained excellent results. We are convinced today, however, that high voltage roentgen rays and filtration through 0.5 mm. Cu is preferable and it is self-evident that when dealing with large bones, such a lesion in the upper extremity of the humerus or the lower extremity of the femur in a large man, the 200 kv. technique is essential.

Our technique in the treatment of giant-cell tumors has always consisted of fractional doses. None of the cases in this series have shown the swelling, increased pain, and marked increase in the decalcified area such as has been reported by Herendeen and Holfelder. We believe that such symptoms are due to the massive dose technique. *In osteogenic sarcoma, rapid*

[1] Pfahler, G. E., and Parry, L. D. Treatment of osteogenic sarcoma by means of irradiation. Am. J. Roentgenol. & Rad. Therapy, 1931, *25*, 761–783.

saturation with radiation to the limit of normal tissue toleration is justified in order not to lose the radiosensitivity, but in giant-cell bone tumors this is not essential and one is less apt to interfere with the repair, or to set up an osteitis. This fact makes an accurate diagnosis essential. Sometimes the prompt improvement which follows irradiation in a young person confirms a doubtful diagnosis. This is illustrated by Case IV reported by Herendeen,[2] a tumor of the heel in a boy aged five, and an exactly similar case in a girl aged twelve (Case II), reported in this series by us. In both these cases the diagnosis was doubtful, and in both, amputation was urged but refused by the parents. Both recovered rapidly, and the foot was restored to normal function.

You will naturally inquire as to the dose, but the answer is difficult and, as Herendeen has said, "It varies with the case." This answer, however, is of no value to the radiologist without much experience. In general, we would recommend treatment with high voltage roentgen rays, filtered through 0.5 mm. of copper, at a distance of 50 cm., 25 per cent skin erythema doses given successively through one, two, three or four fields of entry. If the case is clearly a giant-cell tumor, these treatments need not be given more than three times a week, but if there is any doubt, the treatment should be given daily until the tumor area has been brought to 100 per cent of a skin erythema dose according to the "saturation technique" (Pfahler). If we are satisfied as to diagnosis, the treatment need not be crowded, but in all cases one must keep account of the total dosage, and not give sufficient to produce secondary degeneration. Degeneration effects are due to the total or cumulative dosage and may occur when no erythema has ever been produced. This amount varies with the location, and the condition of the soft tissues. After the treatment during three weeks, one can allow an interval of about six weeks to two months and then re-study the case and treat accordingly.

[2] Herendeen, R. E. Results in röntgen-ray therapy of giant-cell tumors of bone. *Ann. Surg.*, 1931, 93, 398–411.

DAMAGE TO GROWING BONE

The most common site for giant-cell tumors is in the ends of the long bones, and therefore when they occur in young children they are in the neighborhood of the epiphyses. For this reason, many physicians hesitate to have these cases treated by irradiation. However, Borak, after reviewing all of the records, concludes that no normal bone has been found damaged in any of the cases unless there has been some damage to the overlying tissues. This is our experience also. We had damage in one case in which the tumor (a sarcoma) involved the upper extremity of the femur in a child aged one and a half years, in which case there was a recurrence after operation, and after a diagnosis of osteosarcoma, confirmed by microscopy, but there was atrophy and telangiectasis, and fibrosis in the skin. One of our cases of giant-cell tumor has shown interference with growth, but there was also soft tissue damage (Case VI). It is not likely that more than a total of 400 per cent S.E.D. need be given into the tumor, or into any area of skin, and we believe this will not cause damage.

Remarks. Table I gives a brief summary of the results of radiation therapy, but it is impossible to give these results satisfactorily in any tabular form. No two cases are alike, either before or in their response after treatment. In a young person, one finds definite improvement at the end of a month, as is shown in Cases I and II. This is indicated by improvement in the subjective symptoms, and by the deposit of calcium on the inner surface of the cortex as is shown in the roentgenogram. In an older person the improvement in these subjective symptoms also begins in about a month, but one may not be able to demonstrate recalcification until after two, three or even four months. In a young person this recalcification is almost complete at the end of a year, but even after that there is

TABLE I

GIANT-CELL TUMORS

Cases	Region	Date	Age	Sex	Known Duration	Operation	Micro. Report	Tumor Tissue	Condition after Roentgen Therapy
3	Sup. maxil.	1917	23	F	1 year	Resec. (3)	Positive	Yes	Well 13 years.
	Sup. maxil.	1926	20	F	3 months	Curetted	Positive	Yes	Dist. treat. 6 mo. improving.
	Sup. maxil.	1912	10	F	4 weeks	Curetted	Positive	Yes	Well 19 years.
4	Inf. maxil.	1911	7	M	3 months	None	None	—	Well 20 years.
	Inf. maxil.	1914	31	F	9 months	Curetted (2)	Positive	Yes	Well 17 years.
	Inf. maxil.	1922	10	F	4 months	Curetted	Positive	Yes	Well 9 years.
	Inf. maxil.	1925	32	F	4 months	None	None	—	Well 6 years.
3	Clavicle	1916	28	F	1 year	None	None	—	Well 6 years.
	Clavicle	1917	19	M	1 year	Curetted	Positive	Yes	Died of pneumonia 4 mo. after treatment was begun.
	Clavicle	1925	16	F	1 year	None	None	—	Recalcification almost complete after 2 years.
5	Humerus	1922	32	M	1 month	None	None	—	Recalcification almost complete after 9 years.
	Humerus	1925	6	M	3 months	None	None	—	Well 6 years.
	Humerus	1926	3½	F	1 year	None	None	—	Recalcification almost complete after 5 years.
	Humerus	1927	48	M	3 years	Curetted	Positive	Yes	Recalcification almost complete after 4 years.
	Humerus	1929	39	F	12 years	None	None	—	Recalcification 40 per cent at end of 2 years.
1	Metacarpal	1924	31	F	4 months	None	None	—	Recalcification almost complete after 1 year not traceable.
1	Ilium	1909	16	M	5 months	Curetted	Positive	Yes	Well 6 years.
1	Sacrum	1920	24	M	1 year	Curetted	Positive	Yes	Improved 1 year, not traceable.
2	Femur	1921	½	M	3 months	Curetted	Positive	—	Died 3 months, cause unknown.
	Femur	1923	32	M	6 weeks	Curetted	Positive	Yes	Improved 1 year, not traceable.
3	Tibia	1909	23	F	1 year	Curetted	Positive	Yes	Well 22 years.
	Tibia	1925	26	F	1 year	None	None	—	Well 6 years.
	Tibia	1925	15	M	1 month	None	None	—	Recalcification almost complete after 6 years.
2	Fibula	1906	18	F	10 months	Curetted	Positive	Yes	Well 25 years.
	Fibula	1917	18	F	4 months	Curetted	Positive	Yes	Well 8 years, not traceable.
1	Calcaneus	1930	12	F	6 months	None	None	—	Almost well 1 year.

26 Total

contraction in the tumor area. In an old person, this process is much slower, and the tumor area does not contract to the same degree. Therefore, the term "well" means that the patient has complete function, approximately complete recalcification, and one has no reason to fear a recurrence.

This group comprises 26 cases of giant-cell tumor; 61.5 per cent were in females and 38.5 per cent in males. However, this has no special significance unless one is considering injury as a possible cause. Injuries would naturally occur in males more frequently than in females. The youngest patient was six months of age. The oldest patient was forty-eight years of age. The average age is twenty years. Most authorities believe that giant-cell tumors are infrequent under fifteen years of age. In this series, 7 cases, or 27 per cent, were under this age, and of these 7 cases, 3 were referred for postoperative roentgen therapy, and the pathological diagnosis substantiated the roentgen findings.

The average duration of the disease before treatment was 11.4 months. This shows an unnecessary delay which is not always the patient's fault, but many times the physician's. Swollen and painful joints are too often diagnosed as rheumatism, etc., when a thorough history and roentgen study would lead to further investigations and establish a proper diagnosis. However, we are glad to report that in recent years, both the physicians and the laity are more adept and educated along these lines, and seek advice at an earlier date. This has been brought about not only by authentic literature, but by sponsored radio talks, and newspaper propaganda.

According to Kolodny's review, the most common sites of giant-cell tumor are the lower end of the femur and upper end of the tibia (47 per cent), jaws 9 per cent, and spine, 6 per cent. In our series, the tumors in the tibia and femur comprised 5 cases, or 19 per cent; jaws, 7 cases, or 27 per cent; humerus, 5 cases, or 19 per cent; clavicle, 3 cases, or 11 per cent; fibula, 2 cases, or 8 per cent; sacrum, 1 case, or 4 per cent; ilium, 1 case, or 4 per cent; metacarpal, 1 case, or 4 per cent; and calcaneus, 1 case, or 4 per cent.

In this series, 14 cases were operated upon before irradiation was given. The treatment in all cases was administered either for a recurrence or tumor tissue remaining. In our experience with the operative cases, the recalcification following treatment was retarded irrespective of the patient's age, and clearly demonstrated that they respond more rapidly when the tumor tissue is not disturbed or altered. We received a microscopical report in all the cases that were operated upon, but many of them were misleading; for instance, "round cell sarcoma," "giant-cell tumor with spindle cells in the periphery of the growth," "spindle-cell sarcoma with few giant cells." This clearly demonstrates that the roentgenograms are equal, if not superior, to a pathological study, and at the same time, saves the patient from the disadvantages of an operation, which has already been discussed.

Of the 26 cases, 2 are dead; one died of pneumonia four months after treatment was begun, and the other, three months after treatment from an undetermined cause. One case discontinued the treatment six months after treatment was begun; however, the examination showed definite improvement. We were unable to trace 6 of our cases to the present date, but one was followed eight years and 2 cases six years. These 3 cases were well when last examined. The remaining 3 cases were followed for one year. They showed definite improvement when last seen and we believe progressed favorably as all others have done. The remaining 17 cases that are traceable or under observation are "well". There have been no real failures, for all except 2 have been relieved of symptoms, and have had function restored. They have returned to their occupations. The 2 cases which were partial failures had osteomyelitis following operation. One had an amputation of the lower half of the thigh, and the other had a deformed jaw.

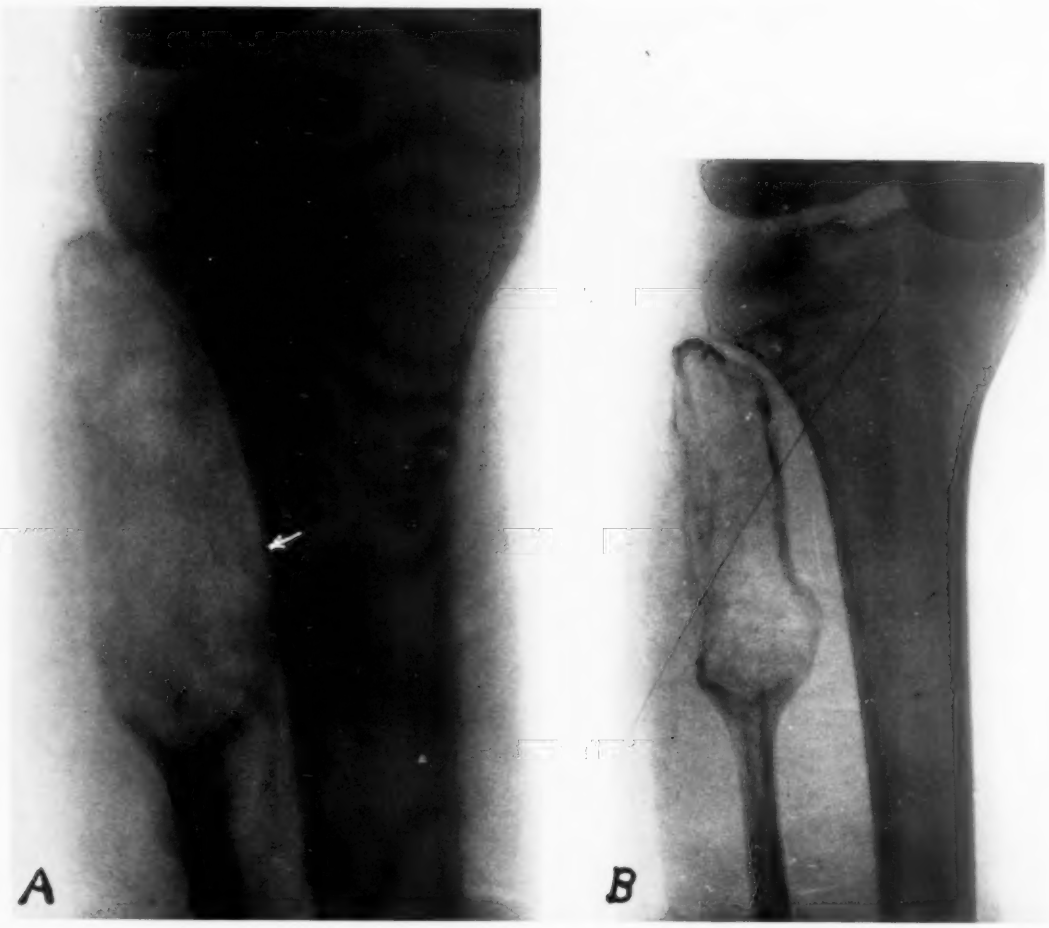

Fig. 1. Case 1. A. Roentgenogram taken on March 5, 1906, shows tumor area involving the upper extremity of the fibula, with complete destruction of all bony structures. The tumor tissue is only slightly more dense than the soft tissue shadows.

B. April 7, 1906. One month after beginning treatment there is a contraction in the tumor area and deposit of a thin shell of bone, scarcely demonstrable, all about the outline of the tumor.

CASE REPORTS

Case 1. (This case was reported under the diagnosis of "sarcoma"—No. VIII—in the *New York Medical Journal*, Dec. 21, 1907.) L.B., female, aged eighteen, was referred to Dr. Pfahler by Dr. M. P. Warmuth, of Philadelphia, on March 5, 1906. She had bruised the upper portion of the leg ten months previously and upon this area a painful tumor developed. On Feb. 20, 1906, a roentgen examination showed the upper 9 cm. of the fibula swollen to a diameter of 3 cm., or three times the diameter of the normal shaft of the bone. The diseased portion apparently contained no lime salts. It showed no medullary cavity, but in its upper portion contained an oval cavity about 1.5×1 cm. in diameter. Otherwise the tumor was uniform in consistency and showed only slightly more density than muscle. A diagnosis of "osteosarcoma" was made. A section was removed for microscopical examination and was reported as "round cell sarcoma."

Amputation at the middle of the thigh was advised, but was refused. Roentgen-ray treatment was then advised and begun March 5, 1906. She was treated six times a week for six weeks, then three times a week. In all, she was given 47 treatments in three months. She has had no treatment since.

A series of roentgenograms were made on March 5, April 7, 1906; August 4, 1907; April 5, 1912; April 10, 12 and 18, 1921, and Novem-

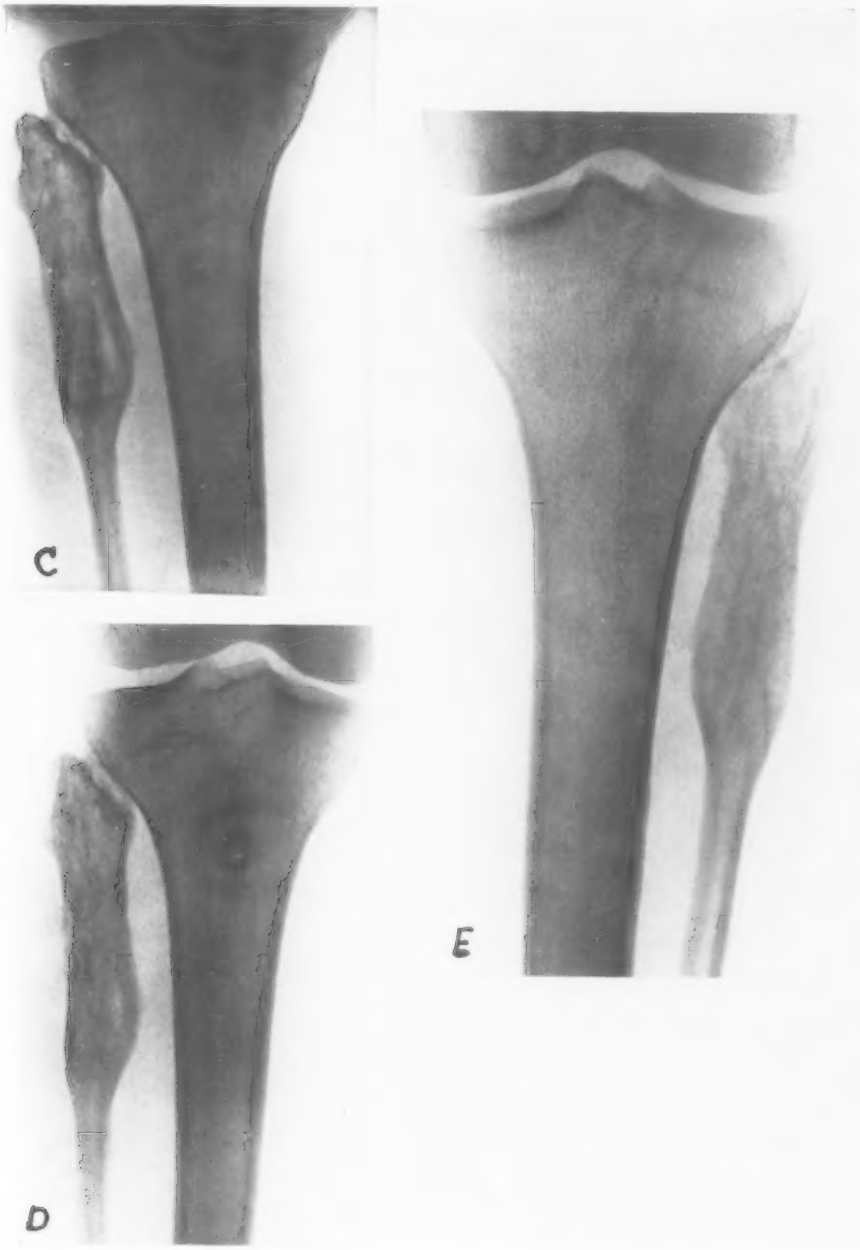

FIG. 2. Case 1. C. Roentgenogram taken on August 4, 1907, over a year after beginning treatment, at which time the patient was symptomatically well, shows about 80 per cent recalcification, and the tumor area contracted to about two-thirds.

D. Roentgenogram on April 5, 1912, shows the tumor area further recalcified, and with more contraction as compared with C.

E. Roentgenogram taken on November 3, 1924, shows the tumor area at least 85 per cent recalcified, with only about 25 per cent increase in size, as compared with the shell of the bone (film accidentally reversed). This series shows particularly the progressive recalcification of this tumor extending over many years. The important period of treatment, however, is during the first month, and usually no treatment is needed after three months.

ber 3, 1924. At that time she was well, and was reported well June 13, 1930, and presumably she is well today (Figs. 1 and 2).

Remarks. This case is of interest because of the following points: (1) We believe it was the first case treated by roentgen radiation. (2) It showed beginning lime deposit at the end of a month, and progressive improvement from that time onward, during at least fifteen years, and is known to be well for twenty-five years. At the end of this time the bone completely recalcified but remained about 25 per cent larger than normal. (3) The clinical, roentgenological, and microscopical diagnosis was "sarcoma," while today we do not hesitate to say definitely it is a "giant-cell bone tumor," based upon the roentgenograms alone. (4) The treatment was given by "low voltage technique" but with an 18 inch coil, a "hard tube" with a platinum target; the dosage was probably about 1/10 S.E.D. (5) The patient continued her usual affairs during treatment and after six months danced several times a week.

Case II (Fig. 3). M.M., female, aged twelve, was referred to the roentgen department of the Graduate Hospital on May 26, 1930, by Dr. W. G. Elmer of Philadelphia. The symptoms started six months previously, with pain in the right heel lasting two weeks and then disappeared. She remained well for two months, when pain and swelling recurred. She was taken to St. Agnes Hospital where local medication was applied, but there was a continuance of pain in the heel extending up the leg at times. She was only able to go about on crutches.

She had been admitted to the Graduate Hospital on May 14, 1930, with a tentative diagnosis of "infected bone in the right foot." On admission on May 26, her temperature was 99.4° F. She had no chills, no cough or night sweats, but some pain in the groin at times. The heel was swollen, painful and tender.

The roentgen examination on May 26, 1930, showed a tumor involving the os calcis, with almost complete destruction of the bone and while it was sharply defined anteriorly, it had broken through into the soft tissues elsewhere. We believed this to be a rapidly growing giant-cell bone tumor, but on account of its having broken into the soft tissues we considered seriously the possibility of osteogenic sarcoma.

After conference, we recommended preliminary roentgen treatment, then a biopsy with permission for amputation if the tumor should prove to be malignant. The parents refused to consent to any form of operation. Our second recommendation was then deep roentgen therapy. We believed, just as Herendeen and his associates believed in a similar case, that even if we succeeded in curing the disease, she would not have a useful leg. Just as in his case, we were pleasantly surprised, for she has normal function and is "well" at the end of a year. After preliminary irradiation an attempt by the needle method to obtain a specimen was a failure and no microscopical examination could be made.

Deep roentgen therapy was given over two fields; 270 per cent skin erythema dose over the inner border of the foot and 290 per cent over the outer border between May 24 and July 25, 1930, according to the "saturation technique." There was also 100 per cent given over the groin. She has had no treatment for more than a year.

Remarks. This case is instructive on the following points: (1) It was an unusual location. (2) There was an interruption of all symptoms during two months. (3) There was suggestive evidence of malignancy. (4) We recommended biopsy and permission for amputation pecause we believed that the limb would be useless even if saved. In this we were mistaken. (5) Improvement was noted in less than a month. (6) There has been no damage to the skin, nor to the epiphysis.

Case III (Fig. 4). W.S., male, aged fifteen, was referred by Dr. R. G. Torrey, of Philadelphia, on October 27, 1925. The patient was admitted to the Medico-Chirurgical Hospital from the Tuberculosis Dispensary on October 1, 1925, with a tentative diagnosis of tuberculosis of the lung. During the examinations, the patient complained of some pain and swelling below the right knee. He gave a history of having injured his knee while playing at school five months previously. He was referred to the roentgen department with the diagnosis of probable osteoarthritis. Roentgen examination of the chest was negative for tuberculosis. A

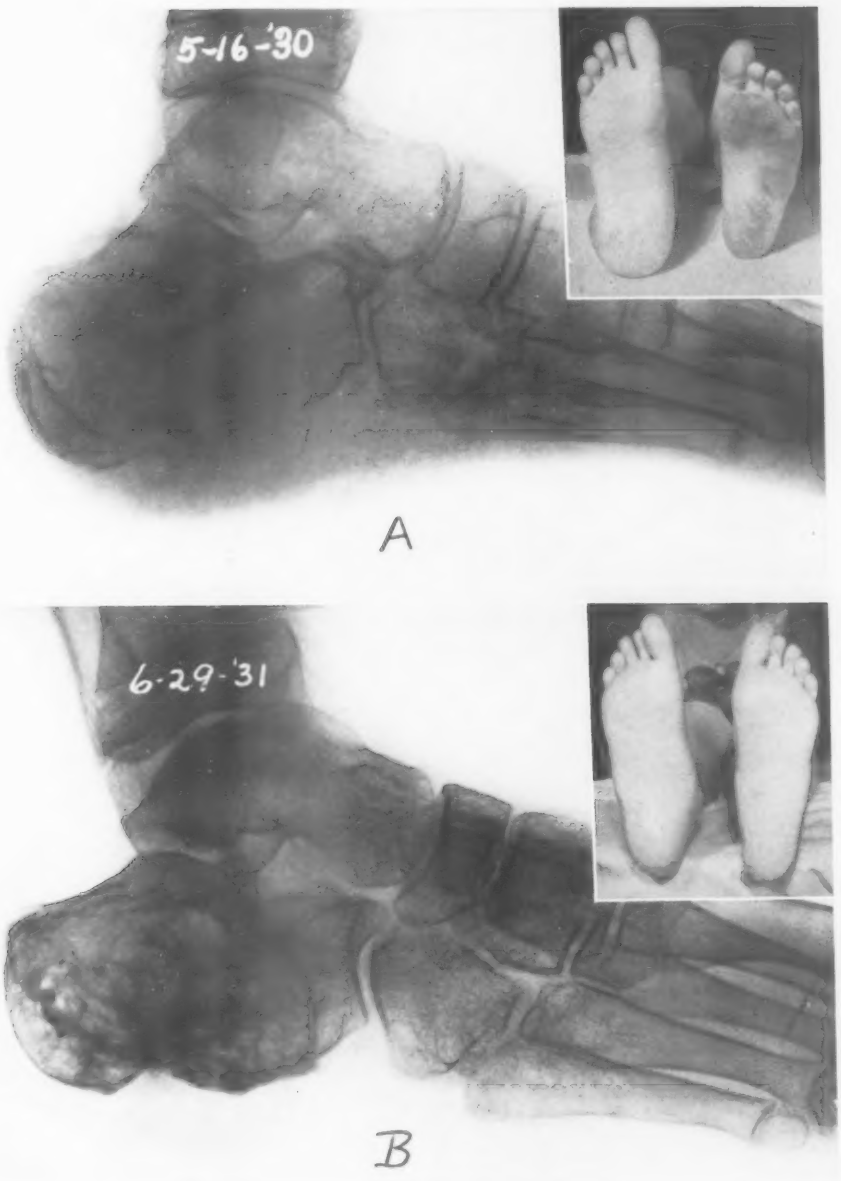

Fig. 3. Case 11. A. Roentgenogram taken on May 16, 1930, shows a giant-cell tumor involving the os calcis but having broken through the capsule, and invaded the soft tissues, associated with much tenderness, swelling and pain. There is also apparently some extension into the soft tissues toward the other carpal bones. This extension made us consider the possibility of osteogenic sarcoma, and we recommended biopsy and possible amputation, which was refused. See photograph of the relative size of the foot and heel at the beginning of treatment.

B. Roentgenogram on June 29, 1931, shows the tumor area almost completely recalcified, and the photograph shows the foot and heel having returned approximately to normal. The patient is walking and is apparently well. This is one of the most rapid results that we have ever seen.

film was made of the knee on October 27, 1925, and a diagnosis of giant-cell tumor was considered, although it was not absolutely certain. In certain areas, the outline of the tumor was sharply defined, but in others, it invaded the bone downward and upward across the epiphyseal line. At the inner and posterior portion, the tumor had destroyed the cortex. This was suggestive of possible osteogenic sarcoma. The patient was given deep roentgen therapy immediately over the inner and outer surface of the knee with the thought of operating later. At the end of three weeks, 145 per cent skin erythema dose had been given on the outer surface, and 185 per cent on the inner surface of the knee.

On November 23, 1925, roentgen examination showed no appreciable change. However, the patient was free of pain. Films were sent to Dr. Codman on December 27, 1925, and his opinion was as follows, dated January 4, 1926, "My guess is in favor of a benign lesion, first, cyst; second, giant-cell tumor. It seems to me that the strong buttress of new bone indicates that the lesion is of long standing, and that such a buttress would only occur in a benign

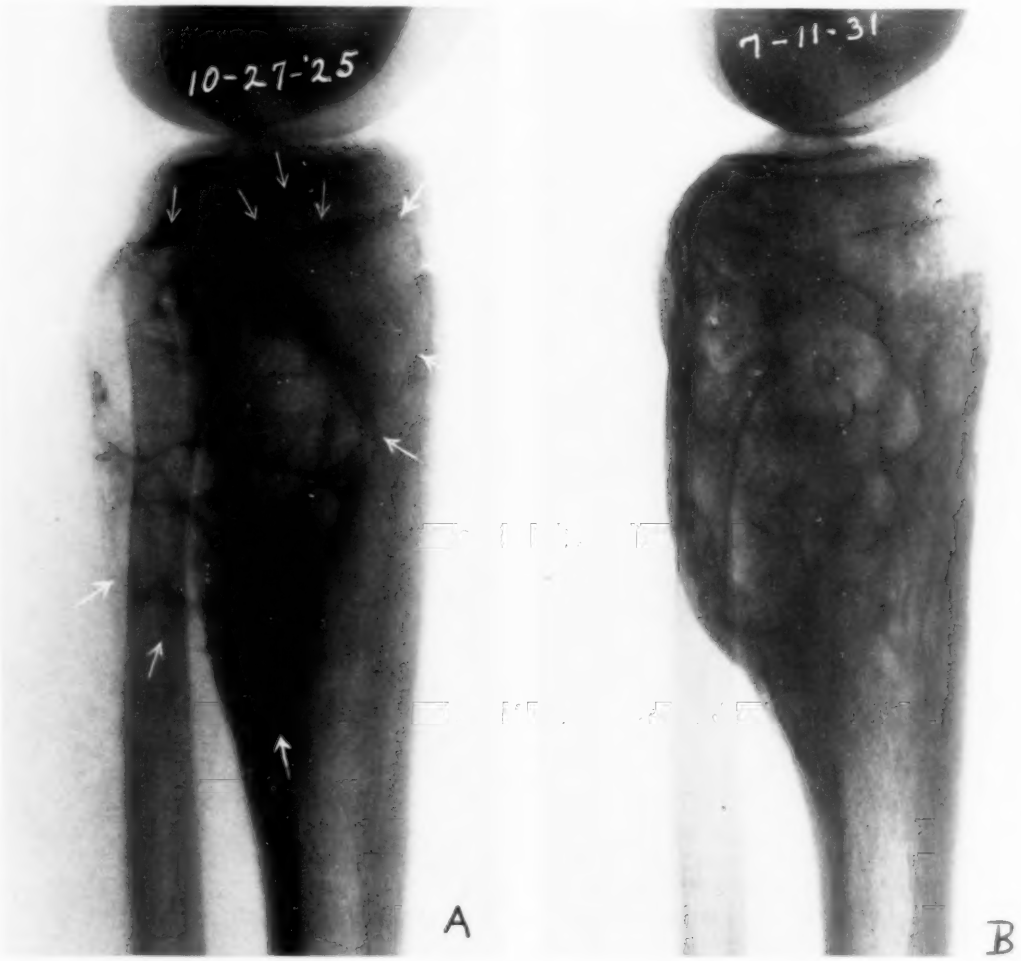

Fig. 4. Case III. A. Roentgenogram taken on October 27, 1925, shows giant-cell tumor involving the upper extremity of the tibia with apparently some extension into the surrounding bone, as is indicated by the small arrows, and which was more clearly shown in the original film. While our primary diagnosis was giant-cell tumor, its appearance gave us some suspicion of malignancy. Operation was refused.

B. Roentgenogram on July 11, 1931, shows the tumor area recalcified to the extent of 75 per cent. This shows slow recovery, but this boy attended school and went about his ordinary affairs from the time of beginning treatment, and for several years has believed himself well.

lesion. It is certainly not an osteogenic sarcoma, which is always both an intra- and extracortical lesion. My only doubt of its being malignant would be hypernephroma. I have seen few instances of the latter which are centrally located and expansive. If there is no enlargement of the renal region by x-ray, this possibility may well be ruled out. It seems to me that x-ray treatment is the treatment of choice, and that it would be unwise to give more than moderate doses for fear of doing more harm than good."

Roentgen therapy was continued and at the end of December 1, 1925, a total of 214 per cent skin erythema dose was given externally on the surface of the knee, and 261 per cent given internally, and a roentgen examination at this time showed gradual and progressive recalcification. No further treatment was given until November 9, 1926, when 100 per cent was given over the inner surface, and 150 per cent over the external surface, during a period of three weeks. Roentgen examinations at various intervals showed gradual recalcification and the patient was free of symptoms. He is perfectly well at the present time and has free use of the limb.

Remarks. (1) This case shows the tumor area overlying the bone in such a manner as to suggest invasion. (2) The pain and subjective symptoms were relieved long before we could demonstrate recalcification. (3) Even though the boy was only fifteen years old the bone repair has been slow, so that after six years the tumor area is only about 75 per cent recalcified. We had judged this as a slowly growing tumor, which may be an explanation. *The patient has been symptom-free after the first three months.*

Case IV (Fig. 5). B.P., female, aged six, was referred for examination and treatment on Oct. 22, 1925, by Dr. Harvey A. Price of Port Carbon, Penna. We obtained a history of a fall three months previously; no fracture was recognized in a roentgenogram made at another institution but showed a tumor. Then six roentgen treatments were given at intervals of two weeks. Further study of the original films by Dr. Grier of Pittsburgh and ourselves showed evidence of a fracture in the tumor area.

A review of the original films and our own made October 22, 1925, showed evidence of giant-cell tumor with fracture in the upper $1\frac{1}{2}$ inches of the shaft of the humerus. Our film showed some evidence of repair.

We gave additional treatment with low voltage roentgen rays amounting to 200 per cent skin erythema dose anteriorly and 120 per cent posteriorly during eight months, ending May 20, 1926. She has had no treatment since. The former diseased area is entirely healed, but as is seen in the illustrations there are some cystic areas below the original area. There has been no interference with bone development.

Remarks. (1) This is a common location for a giant-cell tumor and illustrates how attention is often first called to the tumor by a fracture. (2) It shows complete healing of the tumor area, with complete recalcification, but one can recognize in this area lines which probably come from the fragments. (3) While the original tumor area is healed, there are now small cystic areas lower down. We have seen this in at least one other case.

Case V (Fig. 6). Mrs. E.S., aged thirty-two, was referred for examination on April 6, 1925, by Dr. Wm. Harmer Good, Philadelphia, on account of a tumor in the left lower bicuspid region. It had been growing during four months and was associated with soreness and tenderness, and pain when chewing.

A cystic area about $4\times3\times3$ cm. was found and a diagnosis of giant-cell tumor was made. Roentgen therapy was recommended. We estimated that it would require at least two years for recalcification. Within two weeks the pain and tenderness were relieved. She had also a less conspicuous, and symptom-free swelling of the bone underlying the left nasolabial fold. Roentgen examination showed a similar tumor, less easily demonstrated, in the above-named area. This finding made us think of the possibility of Ewing's tumor. Roentgenograms made from time to time showed after four or five months definite evidence of recalcification, and treatment was discontinued. We re-examined her about once in six months and then once a year, and found the recalcification unusually slow.

On March 17, 1930, after five years, Dr. Albert Finn telephoned me that the patient had fallen a few days previously and had a fracture

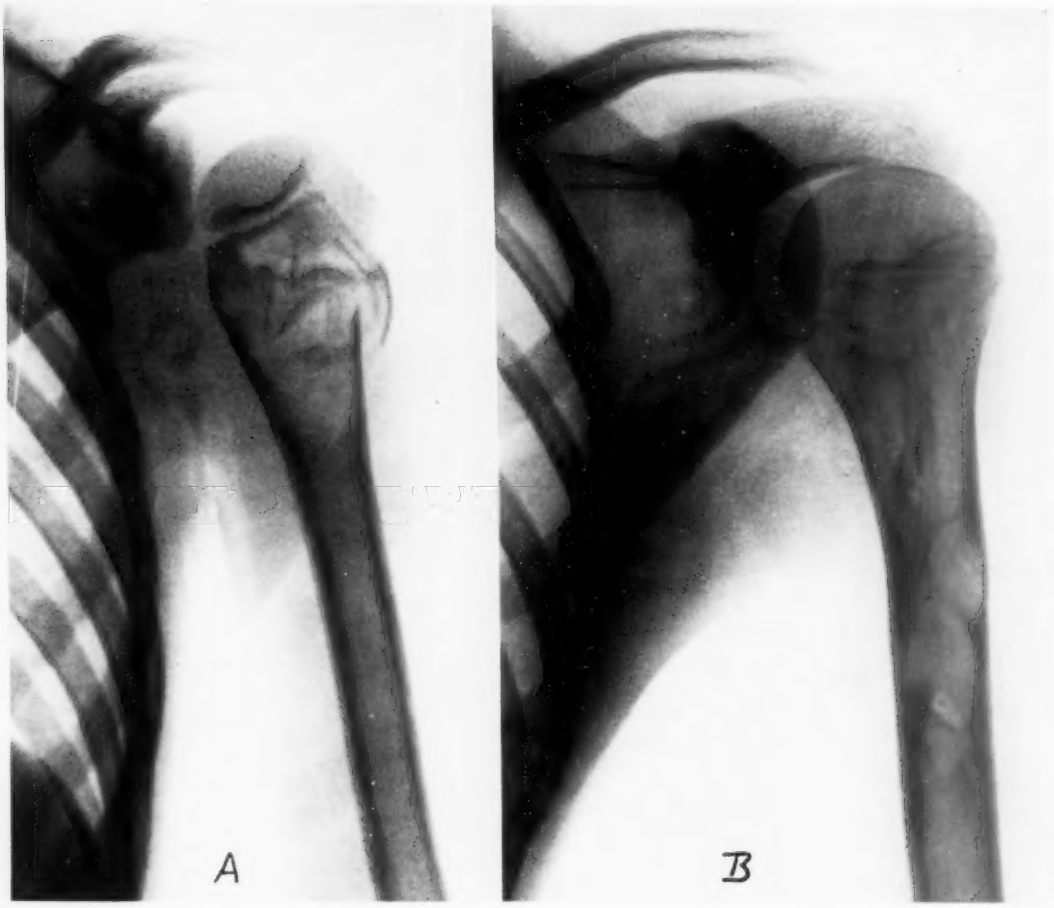

Fig. 5. Case iv. A. Roentgenogram taken on October 22, 1925, shows a giant-cell tumor involving the upper extremity of the shaft of the right humerus, associated with a fracture. The fracture was the first thing to call attention to the tumor area.

B. Roentgenogram on July 3, 1931, shows the tumor area completely healed. Note the striations which correspond to the location of the fracture. There is now evidence of cyst-like areas, probably some tumor cells that have been crowded down by the healing process, entirely below the previous tumor area. No skin damage, no interference with growth.

of the left arm. We made an examination of her arm and found a pathological fracture through the upper extremity of the left humerus at the site of what looked like a giant-cell tumor. We then made a general examination of the bones and found a similar tumor in the lower extremity of the femur, and a more or less general decalcification and many small cystic areas. This led us to suspect parathyroid tumor. She was admitted to the Graduate Hospital. A definite diagnosis of parathyroidism was made, though no tumor was palpable. Dr. Carnett removed a very small tumor, and under appropriate treatment associated with roentgen therapy she has almost completely recovered. This case will be reported in detail later from the standpoint of parathyroidism.

Remarks. (1) This case showed a lesion in the inferior and one in the superior maxilla six years ago. (2) Under irradiation given six years ago there was considerable improvement, but less than has been observed in every other case. (3) A pathological fracture led to the discovery of a giant-cell tumor in the upper extremity of the left humerus, and one in the lower extremity of the left femur. (4) These multiple lesions, together with a general de-

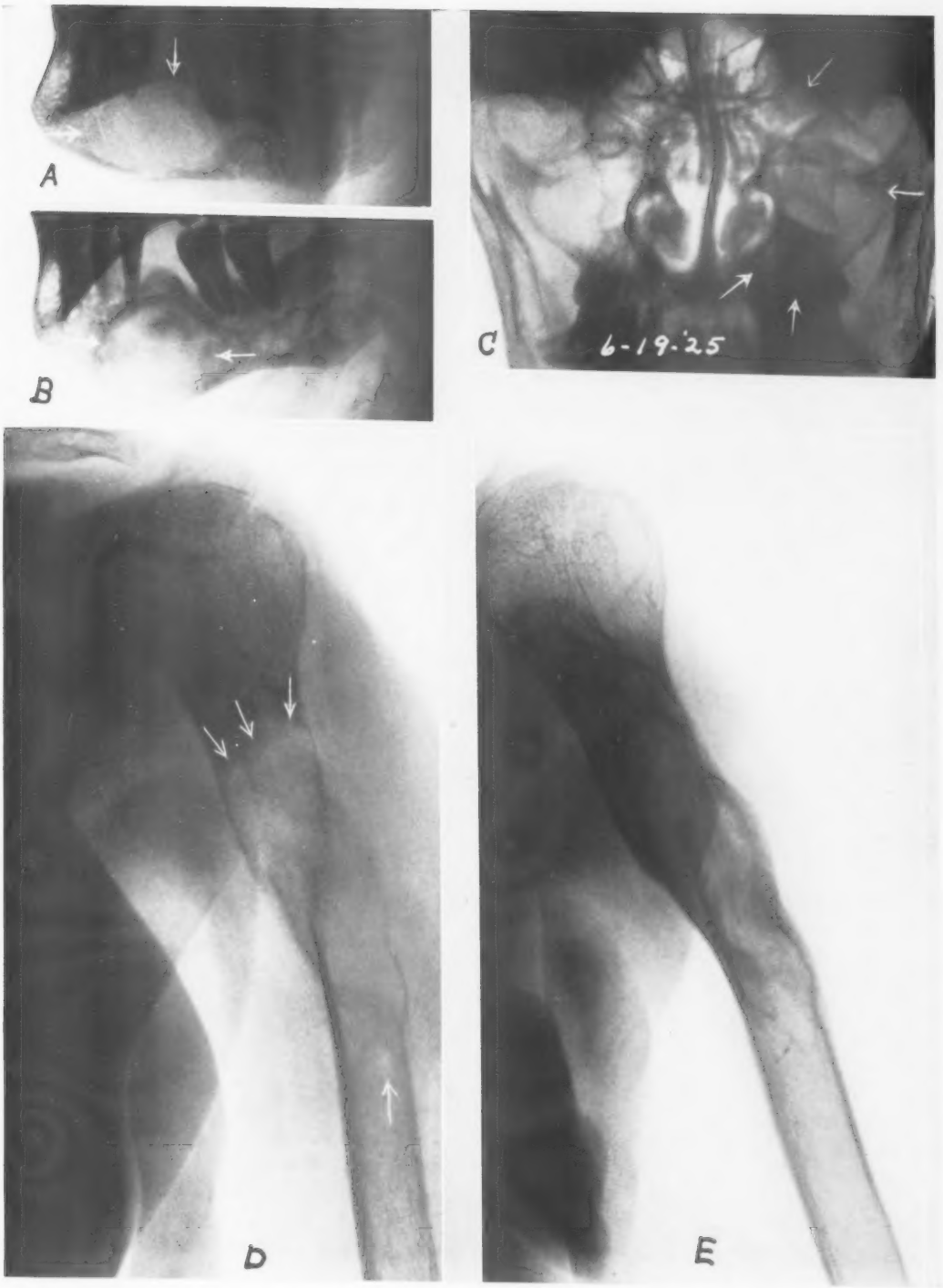

FIG. 6. Case v. A. Roentgenogram on April 8, 1925, shows a giant-cell tumor involving the left lower jaw. B. Shows the same tumor on May 7, 1930, almost healed. This had been more completely healed in previous years, and a new decalcification developed. C. Shows on June 19, 1925, a similar tumor underlying the left nasolabial fold, with opacity of the left maxillary sinus. D. Shows on March 16, 1930, a fracture through a giant-cell tumor in the upper third of the left humerus. E. Roentgenogram on September 30, 1930, shows recalcification of this tumor, and almost normal condition of the bone, following an operation by Dr. Carnett for parathyroid tumor, radiation treatment and calcium and cod liver oil feeding.

calcification of the bones, and the presence of a high blood calcium led to the diagnosis of a parathyroid tumor. (5) Its removal and the administration of calcium, viosterol and roentgen therapy has brought about almost complete recovery.

Case vi (Figs. 7 and 8). B.S., female, aged three and a half, was referred to the roentgen department of the Graduate Hospital, for treatment on January 5, 1926, by Dr. W. G. Elmer of Philadelphia. A roentgen examination was made on August 25, 1925, after a history of injury to the right shoulder four weeks previously. Roentgen examination at that time showed a fracture through the upper extremity of the humerus through a giant-cell tumor. No roentgen treatment was given until January 10, 1926. There was no involvement in this tumor area as a result of the fracture. The tumor involved the upper 7 cm. of the shaft of the humerus.

Fig. 7. Case vi. A. Roentgenogram on January 10, 1926, shows tumor of the upper extremity of the right humerus, involving also the head of the humerus at the beginning of treatment. B. Shows on May 13, 1926, increased growth, and apparently a new fracture. C. On January 28, 1927, with additional treatment, there is evidence of healing to the extent of about 25 per cent.

At the time of beginning treatment, the fracture had healed, but even after beginning roentgen treatment, the healing process was slow, though there was a gradual deposit of lime salts along the edge. There was apparently a second fracture shown May 13, 1926. This line of fracture was still shown January 28, 1927, though with the appearances of healing. When examined on May 21, 1928, the fracture was entirely healed, and there was recalcification to the extent of about 50 per cent. When re-examined September 16, 1931, there was still only about 75 per cent recalcification.

The patient received a total of 500 per cent of a skin erythema dose anteriorly and 500 per cent posteriorly with low voltage roentgen rays, 9 inch spark gap, 5 ma., 40 inch distance, and 6 mm. aluminum filter. To this service dose, one should add at least an additional 100 per cent of an erythema dose from the radiation transmitted from the opposite side. All of this treatment was given between January 10, 1926, and December 24, 1926. The patient disappeared from observation between June 5, 1928, and September 16, 1931, at which time we succeeded in tracing the patient and found she was considered entirely well, was attending school and living a life in every respect like any other girl. We made the following report on that date:

"Patient returns in excellent health. She is going to school; plays baseball, dodge-ball, vol-

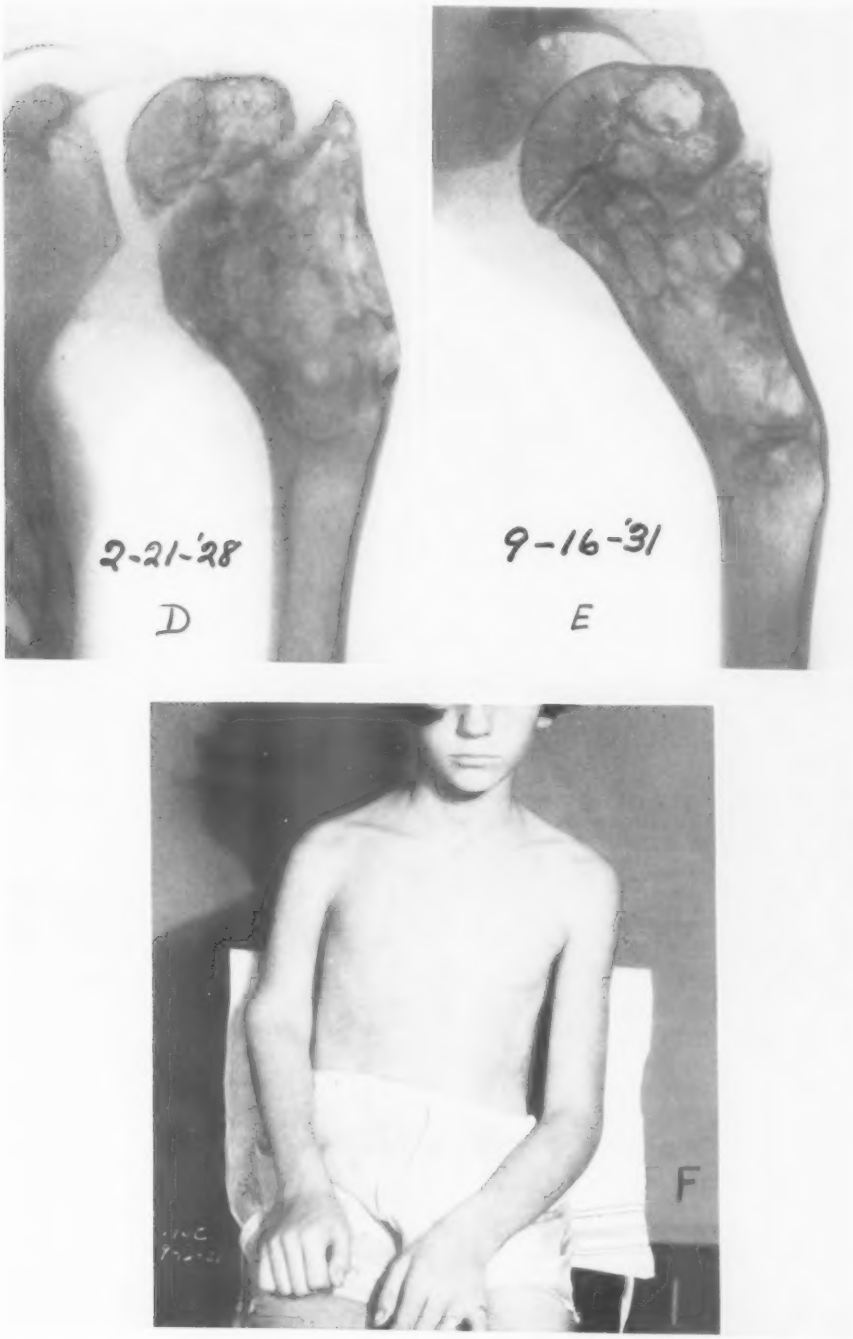

Fig. 8. Case VI. D. Roentgenogram on February 21, 1928, shows recalcification to the extent of about 60 per cent. E. On September 16, 1931, there is recalcification to the extent of about 75 per cent without any treatment since the end of 1926. F. Photograph taken on September 16, 1931, shows the shortening of the right arm, with some atrophy and telangiectasis of the right shoulder.

ley-ball but she says that she throws the ball more crooked with the right arm than with the left; not quite as much power with the right as the left. There is definite atrophy of the right deltoid, and biceps region measures 16 cm. in circumference while the left side at the same point measured 19.5 cm. The right arm is 7 cm. shorter than the left. There is evidence of telangiectasis and some atrophy of the skin anteriorly over the upper extremity of the right arm involving approximately an area 8 to 9 cm. in length. The chest film which was made shows the exact measurements of the bone of the arm on each side as follows: the right humerus measures exactly 18.5 cm., the left measures 26.5 cm. There is therefore a shortening of 8 cm."

Remarks. The interesting features regarding this case are: (1) The patient was symptom-free until the time of fracture. (2) The fracture did not bring about appreciable evidence of healing following roentgen treatment. During the first five months, there was very slight evidence of recalcification. Within the next six months, however, there was about 25 per cent recalcification, and during the remainder—four years—there has been about 50 per cent more recalcification without additional treatment. (3) This patient has definite shortening of the arm, but she also had definite evidence of telangiectasis and atrophy of damage to the soft tissues, bearing out the observation made by Borak that one does not get an interference with the growth of bone unless there is sufficient irradiation to do damage to the soft tissues.

SUMMARY AND CONCLUSIONS

1. This paper is based upon a review of 26 cases of giant-cell bone tumor which have been referred for treatment between 1906 and 1931, covering a period of twenty-five years. The first case is probably the earliest case on record, and was originally considered osteosarcoma.

2. All cases have shown a definite and satisfactory response, more satisfactory in the young than in the old.

3. Two cases died from intercurrent disease. One case had an amputation because of an osteomyelitis following incision, and another developed a deformity of the jaw following similar procedures.

4. We favor fractional doses with high voltage roentgen rays, but not carried to the point of damage to normal tissues.

5. No damage to the epiphyses has been observed.

6. We believe that irradiation is definitely superior to surgery in the treatment of giant-cell tumors of bone. We believe that crushing the bone or curetting it is no advantage, but is rather a disadvantage.*

* For discussion see page 188.

Vol. XXVIII, No. 2

GIANT-CELL BONE TUMOR*

A CONSIDERATION OF THE MORPHOLOGY OF THIS NEOPLASM, THE RESPONSE TO SURGICAL AND RADIATION THERAPY, AND REPORT IN DETAIL OF TWO APPARENTLY MALIGNANT CASES

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THE condition known as "giant-cell bone tumor" has come of recent years to be designated among the majority of American physicians by the term "benign giant-cell bone tumor." Considerable emphasis has been placed on its benign character during this period of particular investigation of bone neoplasms, but the terminology abroad has remained in a large measure that formulated by Nélaton, Paget, and Virchow in the middle of the last century—namely, "tumeur à myéloplaxe," "myeloma," and "myeloid sarcoma." Elmslie has recently acknowledged the objection to the latter two and uses the title of "giant-cell tumour."

The benign character of the lesion is in some minds doubtful. Nélaton in his thesis of 1860 demonstrated the essentially benign character of the "tumeur à myéloplaxe" in the predominating number of cases, even after recurrences. This has been in general the conclusion of Paget, Gray, Virchow, Gross, Bloodgood, Ewing, Codman, Elmslie, and Kolodny. Stone and Ewing, in their review of the literature, did not find any authenticated case of malignant degeneration or of dissemination of true giant-cell tumor metastases. They, however, report a case of at least concurrent malignant bone neoplasm.

The problem of treatment of this lesion has had an almost equal share in the discussion. Paré advised excision of those found in the maxilla. Since then, until the last two decades at least, the preponderant trend has been the surgical attack of the tumor, although somewhat more conservative than radical. Bloodgood and Ewing have perhaps led the conservative van in this country in more recent years. With the advent of radiation therapy there has arisen a controversy as to the respective rôles of surgery and of radiation as therapeutic agents.

It is with the purpose of presenting our reaction in a review of those cases admitted to the University of Michigan Hospital since 1923 that this analysis is arranged in three parts:

(*a*) Incidence of giant-cell bone tumor.
(*b*) Character of the lesion, with the report of 2 apparently malignant cases.
(*c*) The response to various therapeutic programs.

The diagnosis in these cases has been primarily roentgenologic, confirmed in 14 of the 19 cases by surgical material microscopically examined.

(*a*) Incidence. In the last eight years the Department of Roentgenology has made the diagnosis of "giant-cell bone tumor" in 19 cases. This group does not include any with involvement of either maxilla or mandible.

The age of the patients varied from four to forty-nine. The last was a tumor unknown to the patient, an incidental finding in a rib during a thyroid preoperative chest examination. There were 2 in the first decade, 8 in the second, 4 in the third, 3 in the fourth, and 2 in the fifth. Of the 19 cases, 11 were male, 8 female. These figures show a slight variation in age and sex incidence from those of Gross, Bloodgood, and Christensen.

Instead of a preponderance of involvement of the distal portion of the diaphysis of the radius and femur and proximal end

* Read at the Thirty-second Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 22–25, 1931.

of the tibia, as in the collection by Christensen, the distal part of the ulnar shaft is more frequently the site in this relatively small series.

In the matter of the involvement of the "epiphyses" of the bones, as is the common terminology in the older publications particularly, it is of interest that in our series, wherever the epiphyseal discs are still present, the neoplasm has not invaded the disc, being apparently restricted to the end of the diaphysis, the metaphysis. But wherever the epiphyseal disc has been obliterated by maturity of the bone, the tumor proceeds throughout the cancellous structure to the under surface of the articulating cartilage plate.

Only 3 of the series from the University Hospital will be considered particularly. A tabulation in detail of the several cases is appended in Tables I, II, III and IV.

(*b*) The Character of the Lesion.

1. *History and Etiology.* Paré described benign tumors of the maxilla which were cured by excision, Béclard (1827) a medullary, vascular, "not cancerous" bone

TABLE I

GROUP I—CLINICAL CURES

Case No.	Sex	Age Yr.	Year Admitted	Location of Tumor	Time from Alleged Injury to Appearance of Tumor	Microscopic Section	Treatment	Result and Interval between Diagnosis and Last Report
124352	M	21	1925	Radius (D)*	2 yr.	No	Roentgen therapy	Clinically well—5 yr.
133387	M	11	1926	Femur (P)†	4 mo.	Yes	Curettage, acriflavine, roentgen therapy	Clinically well—3 yr.
135259	F	18	1923	Fibula (P)	5 mo.	No	Roentgen therapy	Clinically well—8 yr.
142767	M	15	1926	Ulna (D)	1 yr.	Yes	Curettage, phenol, roentgen therapy	Clinically well—2⅛ yr.
154956	F	34	1926	Femur (D)	4 mo.	Yes	Roentgen therapy, curettage, acriflavine, roentgen therapy	Clinically well—3 yr.
184471	M	18	1927	12th thoracic vertebral spinous process	15 mo.	Yes	Biopsy—roentgen therapy	Clinically well—4 yr.
213022	F	37	1929	Radius (D)	6 mo.	No	Recurrence after surgery, roentgen therapy	Clinically well—3 yr.
222289	M	4	1929	Ulna (D)	—	Yes	Curettage, acriflavine, roentgen therapy	Clinically well—11 mo.
261179	F	4	1931	Humerus (P)	1 yr.?	No	Roentgen therapy	Clinically well—5 mo.
231607	M	18	1929	Fibula (P)	1 yr.	Yes	Excision	No return—patient mentally deficient.

GROUP I (A)—UNTREATED

192750	M	49	1928	7th rib	—	No	Incidental finding—no symptoms	
180985	F	14	1930	Femur (P)	1 yr.?	No	Treatment refused	Diagnosis confirmed elsewhere—3 mo. later.

* (D) indicates distal portion.
† (P) indicates proximal portion.

TABLE II

GROUP II—RECURRENCES

Case No.	Sex	Age Yr.	Year Admitted	Location of Tumor	Time from Alleged Injury to Appearance of Tumor	Microscopic Confirmation	Treatment	Interval of Last Report after Diagnosis
194919	F	36	1928	Ulna (D)	2 yr.	Yes	Roentgen therapy, curettage in 1 month. Recurrence in 6 months. Roentgen therapy resumed—poor response—excision.	15 mo.
203568	F	21	1928	Fibula (P)	2 yr.	Yes	Roentgen therapy for 1 month, did not return for 7 months, roentgen therapy resumed, surgical excision—reason not stated in history.	8 mo.
208025	F	17	1928	Ulna (D)	3 mo. (no trauma known)	Yes	Curettage—recurrence in 6 months. Referred for roentgen therapy 6 months later. Roentgen therapy 4 mo. No report since. Symptomatic improvement.	4 mo.
231254	M	27	1929	Thor. II vert.	7 mo.	Yes	Partial curettage, roentgen therapy. Patient not able to return for adequate treatment—progressive regrowth of tumor.	1 yr.
246845 (Case III)	M	22	1930	Tibia	11 mo.	Yes	Roentgen therapy, curettage in 1 mo. bone chips, progressive growth of tumor in periphery of curetted area—returned for roentgen therapy 9 months later—destruction of bone chips—roentgen therapy resumed (too early for conclusions as to the possibility of accomplishing retardation now).	1 yr.

tumor, and Warren (1837) a benign central tumor of the femur. Lebert (1845) recognized giant cells in certain medullary tumors, and described yellow deposits in these masses as xanthosis, but did not differentiate them from malignant sarcoma. Robin (1849) described two cellular elements of the medulla of bone which he called "cellules medullaires" and "cellules myéloplaques." The former were spherical or polyhedral, 0.015–0.018 mm. in diameter, with a single nucleus of 6–7μ, the cytoplasm granular. They were more abundant in the young than in the old in the interstices between the fat cells and vessels of the bone marrow. The latter type, "cellules myéloplaques," he thought were a minimal normal constituent of adult and aged bone, becoming tumorous when in abundance. They are described as polygonal or irregular spheroids, 0.05–0.08 mm. in diameter, with finely granular cytoplasm containing six to ten nuclei, each of which had one or two nucleoli in their center. These he described first in a case of supposed "spina ventosa," an expansile tumor of the tibia. The term "spina ventosa" had been used also by Dupuytren for a similar lesion along with "fongus hematoïde." Eugène Nélaton considered that Robin deserved credit for the real identification of the "myéloplaques" as normal minor constituents of bone marrow. Lebert and Müller had called the giant cells "mother cells"; Kölliker considered them osteoclasts.

Nélaton in his thesis of 1860 offered a

simple but none the less adequate definition of this neoplasm—"tumeur à myéloplaxes (ou tumeur myéloplacique)"—a particular kind of accidental tissue production whose fundamental architecture is characterized, not by simple presence of, but by the predominance of the anatomic elements called "myéloplaques."

From this point he proceeded to indicate four essential types of this class of tumor: (1) the solid or meaty (typical); (2) the fibroid, with more fibroblastic proliferation in the stroma; (3) the "graisseuse" or xanthoid, and (4) the vascular. The cystic changes not uncommonly seen were considered as simple degeneration of the tumor. Such as showed hemorrhage into these cystic areas were considered the result of natural extravasation from the new-formed vessels of the tumor (probable so-called bone aneurysm).

Table III

GROUP III—APPARENT MALIGNANT DEGENERATION

Case No.	Sex	Age Yr.	Year Admitted	Location of Tumor	Time from Alleged Injury to Appearance of Tumor or Symptoms	Microscopic Confirmation	Treatment
251075 (Case 1)	M	17	1930	10th rib	3 mo.	Yes	Roentgen therapy, surgical excision, cardiac death 24 hr. postoperative. Spindle-cell sarcoma arising in giant-cell tumor of rib and invading soft tissue.
253116 (Case 11)	M	45	1930	pelvis	6 mo. Known tumor for 20 yr., rapid increase in last 9 mo.	Yes	Biopsy of tumor left ilium. Roentgen diagnosis of pulmonary metastatic neoplasm. Roentgen therapy pelvis and chest for relief of pain and dyspnea, improvement, alive but weak, has not returned since initial therapy—7 mo.

Gross (1879) refuted Robin's theory of the source of the giant cell from a normal cell of the bone on the basis of age prevalence of the tumor in the third decade, beyond the usual period of common appearance of these cells in normal marrow. His idea of the etiology projected a reversion of the marrow to a fetal state upon irritation or trauma, with a resultant rapidly growing process in which bone substance is lost, associated with freedom from bone repair following rupture of a nutrient artery.

One might continue speculating, wavering between the school of the neoplasm, of the rather simple inflammatory process, of the equally simple and perhaps more logical repair after rupture of continuity and hemorrhage, or of the more theoretical linkage with osteitis fibrosa cystica, parathyroid deficiencies, and so forth. In almost every case of this series it has been of interest to hear the patient's own allegation of origin in some trauma, which may range from a slight twist of the wrist to a blow from falling timber with resultant dislocation of the hip.

At any event the essential cell constituent, the multinuclear giant cell, has not changed in character since Robin and Néla-

Mallory has considered the process as a reaction of the large mononuclears—endothelial leucocytes—with fusion, and an associated loss of calcium salts, the remainder of the cell content of the lesion being common to the ordinary inflammatory reaction. Codman in a measure joins him with the belief that it largely represents a

ton—a large cell with many centrally situated nuclei.

2. *Micropathology*. We prefer to confine our qualification of the neoplasm to that given by Ewing—a process which is characterized by a sharply demarcated central tumor of bone in which large multinucleated giant cells predominate, either through the whole mass or in scattered masses. These cells may enclose blood and cell detritus, bony granules, or lipoid. There are many fine capillaries, and a spindle-celled stroma, sometimes cystic spaces with bloody fluid. Bone formation is not common save at the periphery, and cartilage is occasionally found in islands, which are considered isolated remnants of the epiphyses and undergoing destruction by the tumor. It is an essentially benign neoplasm, but on repeated irritation by surgical or other trauma, may show progressive development of increased cellular

TABLE IV

MICROPATHOLOGY

Case No.	Age Yr.	Location	Description of Section
124352	21	Radius	No specimen.
133387	11	Femur	Giant-cell bone tumor, very cellular, spindle-cell stroma, no new bone.
135259	18	Fibula	No specimen.
142767	15	Ulna	Giant-cell tumor developing in area of old osteitis. Very cellular stroma about giant-cell areas. Necrosis and absorption of bone.
154956	34	Femur	Benign giant-cell neoplasm, extensive necrosis, dense fibrous stroma, some bony trabeculae.
184471	18	12th d. vertebra	Very vascular granulation tissue containing many giant cells; large aneurysmal blood spaces lined by giant cells; some new bone formation beneath the periosteum. So-called bone aneurysm in giant-cell tumor.
213022	37	Radius	No specimen.
222289	4	Ulna	Regeneration of bone about a thin wall of older bone, within this a cavity lined with benign giant-cell tumor, bone aneurysm in giant-cell tumor.
261179	4	Humerus	No specimen.
231607	18	Fibula	Typical giant-cell tumor; some hyaline areas; absorption of old bone.
192750	49	7th rib	No specimen (may be an osteochondroma).
180985	14	Femur	No specimen.
194919	36	Ulna	Very cellular benign giant-cell tumor, large necrotic areas bordered by disintegrated cells and very large giant cells, some with apparently 50 nuclei, protoplasm vacuolated, some hemorrhagic zones. After roentgen therapy and excision, more compact with more uniform cell size.
203568	21	Fibula	Very cellular benign giant-cell tumor, necrotic areas, much chromatin dust. After roentgen therapy and excision, more compact giant-cell tumor with osteoid tissue and areas of regeneration of bone—probably reparative.
208025	17	Ulna	(Biopsy elsewhere 1 yr. before admission—section available.) Giant-cell tumor with very cellular spindle-cell stroma; some large round cells.
231254	27	Vertebra—Th. II.	Very cellular giant-cell tumor, solid cords of giant cells, large capillaries, giant cells staining rather deeply.
246845 (Case III)	22	Tibia	(One month after beginning roentgen therapy.) Giant-cell tumor with enormous numbers of very large giant cells, some areas very vascular, others necrotic, hemorrhagic, giant cells near. Necrotic areas show pycnotic nuclei, vacuolization of protoplasm, cell death—probably response to roentgen radiation.
251075 (Case I)	cited in detail in body of paper.		
253116 (Case II)			

TABLE V

TREATMENT SCHEDULES*†

Group I 124352	Roentgen therapy only	Radius (D)	130 kv. peak, 30 cm., 0.25 mm. Cu, 1.0 mm. Al, 50–10 per cent S.U.D., ant. and post., gradually lengthening intervals from 2 wk. to 4 mo., from 1925–1928; 130 kv. peak, 30 cm. distance, 4.0 mm. Al, 125 r ant. and post. wrist at 5 mo. intervals, 1929–1930.
133387	Curettage, acriflavine, roentgen therapy	Femur (P)	200 kv. peak, field 50×50 cm., 0.5 mm. Cu, 1.0 mm. Al, ant. and post., 50–10 per cent S.U.D., intervals of 2–6 mo. from 1926–1928.
135259	Roentgen therapy only	Fibula (P)	200 kv. peak, 50 cm. distance, field 10×10 cm., 1.0 mm. Cu, 1.0 mm. Al, ant. and post., 50–60 per cent S.U.D.; 200 kv. peak, 50 cm. distance, field 10 ×10 cm., 1.0 mm. Cu, 1.0 mm. Al, lateral, 25–30 per cent S.U.D., 3 mo. intervals, 1923–1924. 200 kv. peak, 50 cm. distance, field 10×10 cm., 0.5 mm. Cu, 1.0 mm. Al, ant. and post., 10–25 per cent S.U.D. in 3 mo. intervals, 1927–1928; none since.
142767	Curettage, phenol, roentgen therapy	Ulna (D)	130 kv. peak, 30 cm. distance, 0.25 mm. Cu, 1.0 mm. Al, ant. and post., 50–10 per cent S.U.D., intervals of 1–2 mo. 1926–1927.
154956	Curettage, acriflavine, roentgen therapy	Femur (D)	200 kv. peak, 50 cm. distance, field 20×20 cm., 0.5 mm. Cu, 1.0 mm. Al, ant. and post., 50–10 per cent S.U.D., decreasing doses at monthly intervals, October, 1926–April, 1927; one in July, 1927—200 kv. peak, 50 cm. distance, 0.5 mm. Cu, 1.0 mm. Al, medial and lateral, 15 per cent S.U.D.
184471	Roentgen therapy	12th thoracic vertebra	200 kv. peak, 50 cm. distance, field 20×20 cm., 0.5 mm. Cu, 1.0 mm. Al, 35–15 per cent S.U.D., series of 3 doses (35 per cent S.U.D. each) on April 16, 17, 18, 1928, decreasing doses monthly intervals June to December, 1928.
213022	Roentgen therapy only	Radius (D)	130 kv. peak, 30 cm. distance, 4.0 mm. Al, ant. and post, 200–100 r, monthly intervals, 1929; 120 kv. peak, 30 cm. distance, 4.0 mm. Al, ant. and post, 125–75 r monthly to trimonthly intervals, 1930–1931. Last treatment March 25, 1931.
222289	Curettage, acriflavine, roentgen therapy	Ulna (D)	Roentgen therapy elsewhere, no data available.
261179	Roentgen therapy only	Humerus (P)	120 kv. peak, 30 cm. distance, 4.0 mm. Al, ant. and post, 200–250 r, monthly intervals, April–September, 1931.
Group II 194919	Roentgen therapy 1 mo. curettage, recurrence 6 mo. Roentgen therapy resumed—excision	Ulna (D)	130 kv. peak, 30 cm. distance, 4.0 mm. Al, ant. and post., 25–50 per cent S.U.D., bimonthly intervals, June, 1928–November, 1929; 130 kv. peak, 30 cm. distance, 4.0 mm. Al, ant. and post., 100 r, Feb. 7, 1929; 200 kv. peak, 50 cm. distance, field 15×15 cm., 0.5 mm. Cu, 1.0 mm. Al, ant. and post., 100 r, June 20, 1929; 130 kv. peak, 30 cm. distance, 0.25 mm. Cu, 1.0 mm. Al, ant. and post., 15 per cent S.U.D., Oct. 31, 1928.
203568	Roentgen therapy 1 mo. curettage—returned. Roentgen therapy resumed—excision.	Fibula (P)	130 kv. peak, 30 cm. distance, 2.0 mm. Al, lateral, Nov. 30, 1928, 200 r; 4.0 mm. Al, lateral, Jan. 3, 1929, 100 r; 4.0 mm. Al, anterior, March 11, 1929, 100 r.

TABLE V (*Cont.*)

TREATMENT SCHEDULES*†

Group II			
208025	Curettage—recurrence 6 mo. Roentgen therapy started 6 mo. later for 4 mo. No later report	Ulna (D)	130 kv. peak, 30 cm. distance, 4.0 mm. Al, 200 r ant. and post.
231254	Laminectomy to relieve pressure on cord from vertebral bodies	Thor. II vert. body	Returned to home physician for roentgen therapy.**
24685 (Case III)	Cited in detail in body of paper.		
Group III 251075 (Case I) 253116 (Case II)	Cited in detail in body of paper.		

* On basis of recalibration (1928) in roentgens of 200 kv. peak energy with 0.5 mm. Cu and 1.0 mm. Al filter, 1 S.U.D.=500 r approximately.

† On basis of recalibration (1928) in roentgens of 130 kv. peak energy with 4.0 mm. Al as above. 1 S.U.D.=400 r approximately.

** July, 1932. Record of patient since return home has been traced with report from his physician that under roentgen therapy patient has now returned to his work with almost no disability.

proliferation with perhaps ultimate transition of a part into a true malignant neoplasm capable of dissemination and growth.

3. *Roentgen Pathology*. The roentgenographic characteristics of this lesion of bone have been rather well established as a central osteolytic tumor near the end of the diaphysis tending to produce distortion of the normal bone contour by expansion, progressively destroying the normal architecture of the bone with an attempt by the periosteum to maintain an unbroken shell of cortex. The tumor seems to be confined by the periosteum, is more or less trabeculated by bony "cross-members," and is not traversed by the old shaft. These latter set the giant-cell tumor off rather distinctly from osteogenic sarcoma.

From the roentgenologic standpoint, it matters little in diagnostic differentiation whether one is dealing with the more typical variety of giant-cell tumor, the xanthoid, the aneurysmal, or the chondrogenic type. In the examination of the films of a new case, the roentgenologist should not attempt to differentiate between these. Perhaps he may if reviewing a series on the patient.

It seems to be a disease of the metaphyseal end of the diaphysis. We have not seen a case in which we would make a diagnosis of giant-cell tumor where the epiphyseal disc, if present, has been invaded by the tumor.

I am further of the opinion that the microscopic section would not show a predominant character of osteitis fibrosa cystica when a single lesion of the skeleton is found, although the cortical bone seems somewhat condensed and fibrotic, and the trabeculae numerous in certain cases. The fibrocystic changes should represent a degenerative process of more extensive nature.

Analysis of this series of cases does not permit an entry into the more or less current discussion of whether or not there is a common etiology for the bone changes in osteitis fibrosa, giant-cell bone tumor, xanthosis, parathyroid dystrophy, etc.

These 19 cases presented, in our opinion (and, when tissue specimens were available, in the opinion of Doctors Warthin and Weller), the roentgenologic and pathologic characteristics which we have stated above. Table IV presents the micropathol-

Fig. 1. Case 1 (251075). Preoperative pneumothorax. Shows soft tissue mass in the region of partially destroyed left tenth rib.

ogy in somewhat more detail. It will be noted that two exhibited cystic degeneration with hemorrhage to a degree which permitted a diagnosis by the pathologist of bone aneurysm. Yet the roentgen appearance did not offer appreciable variation to warrant such an opinion in distinction from the others.

4. *Possible Malignant Degeneration.* Stone and Ewing in 1923 reported a case of giant-cell tumor in which there appeared a general neoplastic metastasis. In this connection, 2 cases—Nos. 251075 and 253116—present certain features which we believe warrant consideration in detail:

Case 1 (No. 251075). White schoolboy, aged seventeen. Admitted October 10, 1930, with the story of a blow on the posterolateral lower left chest while playing basketball nine months before. It was considered as a fractured rib and treated with adhesive strapping. No roentgen study. Swelling appeared one month after injury with gradual increase in pain and size of tumor. Loss of 20 lb. in weight in the nine months. Dry cough.

Examination. A palpable mass, elevated about 2 inches, and about 6 by 8 inches in area, presented over 10th and 11th ribs left posterior axilla. Mass firm and apparently fixed to bony wall. Skin not fixed. No gross hyperemia.

Roentgen examination October 10, 1930. Lung fields clear, heart normal, slightly to left. Destructive lesion posterior portion left 10th rib, pressure atrophy of upper margin 11th. Suggestive of destructive neoplasm (Fig. 2*a*).

Roentgen therapy instituted October 13, 1930: 200 kv. peak, 50 cm. focus skin distance, 20×20 cm. field, 0.5 mm. Cu, 1.0 mm. Al, 150 r.

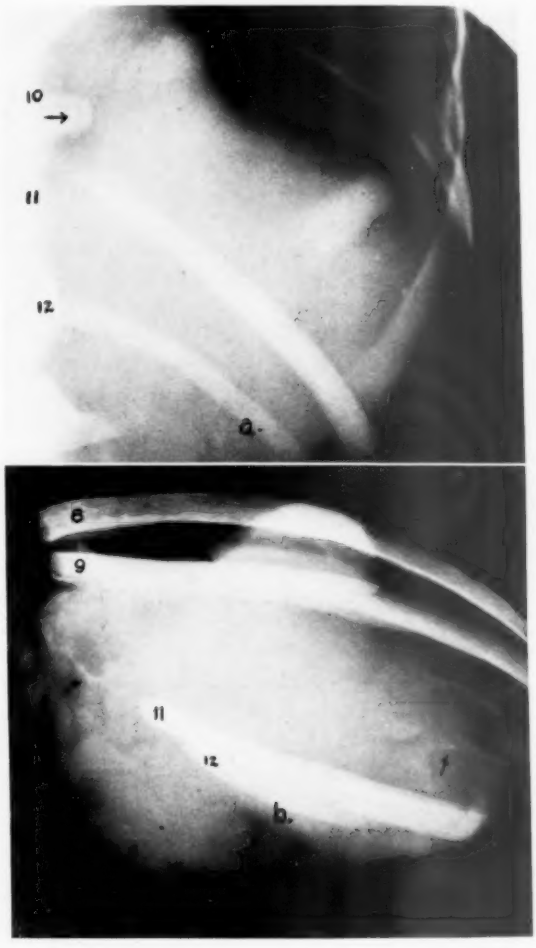

Fig. 2. Case 1. (*a*) Detail showing destruction of posterior portion of tenth rib, small fragment remaining at articulation with vertebral transverse process, soft tissue tumor mass.

(*b*) Surgical specimen, November 28, 1930. Tenth rib partially re-ossified forty-two days after roentgen therapy; suggests expansile tumor, rather trabeculated where ossified; soft mass in center.

This dose was repeated to the posterior chest wall on October 14, 15, and 16. Total, 600 r. Patient returned November 13, 1930—same dose repeated. He reported at that time decrease in size of tumor, gain in weight, and loss of pain.

Roentgen examination November 13, 1930. Apparent expansile tumor of 10th rib as shown by anterior margin in rib fragment, not the appearance of an osteogenic sarcoma. After pneumothorax for diagnosis and preoperative treatment, the report was a "tumor mass, shape of thumb, projecting into thoracic cavity from soft mass arising in 10th rib" (Fig. 1).

Thoracotomy November 28, 1930. Ribs 8 to 12 sectioned in anterior axillary line and at costovertebral junction and removed *en masse*. Tumor mass as seen on films. Lower lobe of left lung adherent to it over an area 5×5 cm. No palpable evidence of neoplastic invasion of lung, wound closed, patient in good condition.

Roentgen examination of surgical specimen: November 29, 1930—expansile loculated character of 10th rib at either side of tumor mass. Suggests giant-cell tumor more than osteogenic sarcoma (Fig. 2*b*).

November 29, 1930—Rapid drop in blood pressure with increase in pulse rate. Patient did not respond to treatment. Death 2:25 A.M., November 30, 1930, forty hours postoperative.

Autopsy: Persistent thymus, thymico-lymphatic constitution—surgical wound left posterior thorax with loss of last 5 ribs posteriorly—no evidence of neoplastic metastases.

Histopathology of surgical specimen: "A combination of osteogenic sarcoma and giant sarcoma arising in giant-cell tumor"—Warthin. After decalcification—"Chondro-osteogenic sarcoma arising in giant-cell tumor of the rib infiltrating bone and surrounding tissue. Some new formation of bone and cartilage other than that in the neoplasm." Weller. (Figs. 3 and 4.)

If we should assume a previous proper diagnosis of fracture of the rib, there may in this case be a definite origin for the giant-

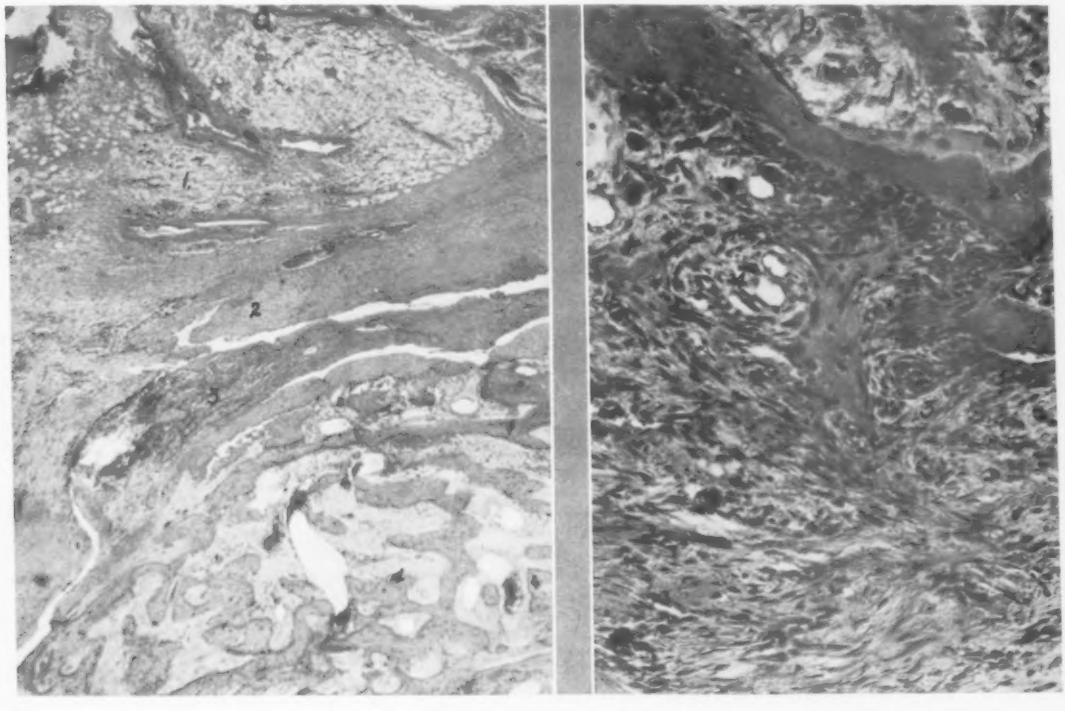

Fig. 3. Case 1. (*a*) Photomicrograph (low power) showing (1) compressed lung bordering tumor; (2) thickened visceral pleura; (3) parietal pleura with very cellular connective tissue, some attachment to parietal pleura, no invasion, and (4) osteoid periphery of tumor mass.

(*b*) Photomicrograph (higher magnification) of more central portion of tumor with (1) giant-cell tumor margin; (2) osteoid formation; (3) very cellular stroma, spindle cells in whorls, cells rather abnormal, and (4) prominent vascular channels.

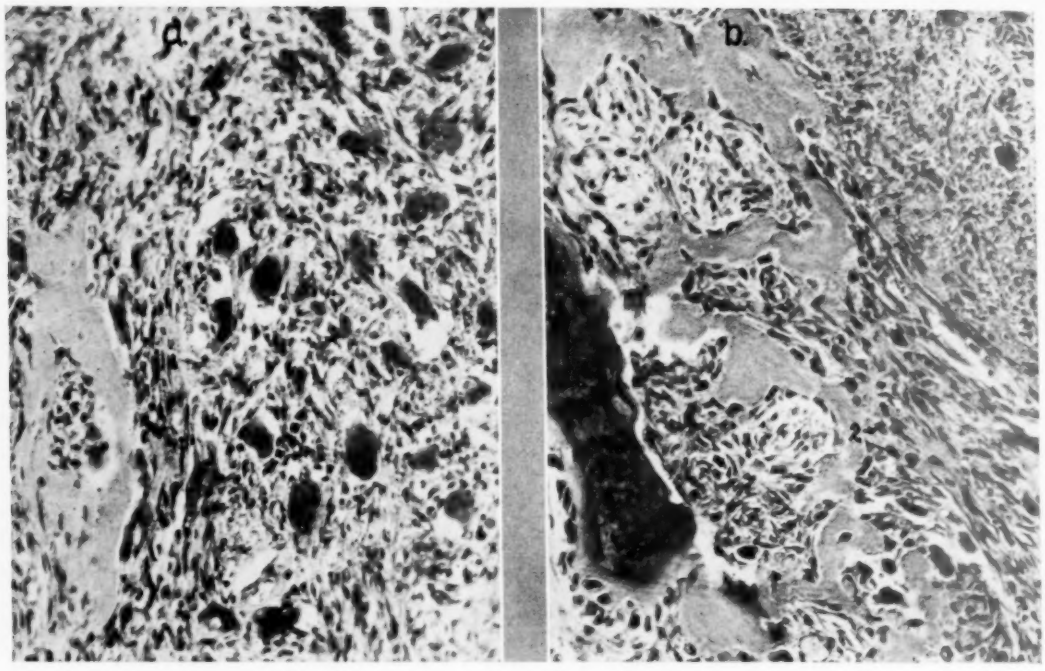

Fig. 4. Case 1. (*a*) Photomicrograph of more typical giant-cell areas of tumor, nuclei of giant cells numerous and centrally placed.

(*b*) Field contiguous to that of (*a*) showing more typical giant-cell type of tissue in upper right (1) with transition to more irregular spindle-cell stroma with osteoid and calcareous masses in middle and left portions. Nuclei hyperchromatic, deeply staining cytoplasm, some suggestion of cell division (2).

cell bone tumor referable to trauma. We then are faced with the necessity of developing a theory of degeneration of the giant-cell tumor during the nine months, or of the spontaneous "naissance" of the osteogenic sarcoma in the same area. The preponderance of the typical "bone tumor giant cell" in multiple sections of this mass is adequate to warrant a conclusion of primarily a giant-cell bone tumor, secondarily, the sarcoma. The pleura had become adherent as is seen in the photomicrograph (Fig. 3*a*) but not infiltrated. There were masses of giant cells interspersed with very cellular stellate and spindle-cell areas (Figs. 3*b* and 4), some osteoid and osseous tissue, some areas of necrosis. The latter, in part we believe, may have been associated with the response to roentgen therapy although only six weeks had elapsed since its institution. Hence from the point of view of time for response, the case could still be in the immediate osteolytic phase. Yet the films of the specimen demonstrated definitely trabeculation which at least had not been seen the month before (perhaps because of overlying soft tissue).

I do not believe one should presume any further conjecture as to the relation between the giant-cell tumor and the sarcoma. They were concurrent at the time of section—probably the giant-cell tumor had preceded the other.

Case II (No. 253116). White, male, laborer, aged forty-five. Admitted November 11, 1930, with complaint of a painful mass on left hip. Injured 1911 by falling timber, diagnosis-dislocation of the left hip, incapacitated for two weeks. Six to eight months later he noticed a severe sharp pain in the hip; no roentgen study; no diagnosis. Constant pain relieved in about a month, but weight-bearing was painful. Two months later patient noticed tumor on inside left thigh (in crotch) (said he was admitted to the hospital, 1912, but record cannot be

checked). No biopsy known. Tumor and pain decreased. In 1914 tumor began to grow again in left buttock; "light treatments"; tumor decreased, he returned to work; no gross disability. In February, 1930, he fell on left hip and back. Pain returned and with it a rapid increase in size of tumor and amount of pain. Left leg now numb and somewhat swollen; loss of 10 lb. since February, dry cough, marked weakness.

Examination: Large tender mass left lateral buttock, left crotch, and left lower quadrant of abdomen, extending medially to near the umbilicus. Almost complete restriction of motion left hip, thigh and leg edematous; muscle atrophy. Telangiectatic area left buttock (possibly previous roentgen therapy described by patient as "light treatments").

Roentgen examination November 11, 1930, demonstrated lobulated expansile tumor of left ilium and ischium, large mass in medial portion of thigh. Cortical layer of bone apparently intact over lower masses. Tumor of ilium shows apparent loss of cortical bone in lateral upper thigh and over crest. Appearance suggests giant-cell bone tumor with apparently rapidly growing, more malignant upper portion as of a chondrosarcoma (Fig. 5).

Fig. 5. Case 11 (253116). Gross giant-cell bone tumor of the innominate bone; origin probably sixteen years before; recent rapid increase in size; apparent active destruction in ilium with few trabeculae; older tumor apparently in ischial portion; old fracture of the neck of the femur.

Fig. 6. Case 11. Multiple round soft masses in both lung fields and hilum which are interpreted as neoplastic metastases—from pelvic tumor.

The roentgen study of the chest showed multiple round soft tissue masses about 2 cm. in diameter lateral to the left hilus and smaller similar areas scattered through the right lung field. These are the type usually found in metastatic sarcoma (Fig. 6).

Biopsy November 13, 1930, from left ilium. "Marked vascularity, impossible to control hemorrhage by ligature—wound packed." Tissue reported, "giant-cell tumor with high degree of cellularity." Weller. The section material (Fig. 7) shows a fibrous capsule about a tumor mass with small round cells and many typical giant cells with pale protoplasm and multiple (but few) central nuclei, suggesting a rapidly growing tumor; no pleomorphism; no hyperchomatism; no excess mitosis in the giant cells.

Roentgen therapy (with intent of palliation only) over pelvic tumor was instituted November 22, 1930: 190 kv. peak, 50 cm. focus skin distance, 0.5 mm. Cu, 1.0 mm. Al, 15×15 cm. field, 150 r each, anterior ilium and left gluteal, and repeated on November 24 and 26, with relief of pain. December 9, 11, and 13, 75 r (of the same quality of radiation) was administered over the anterior right and left lung

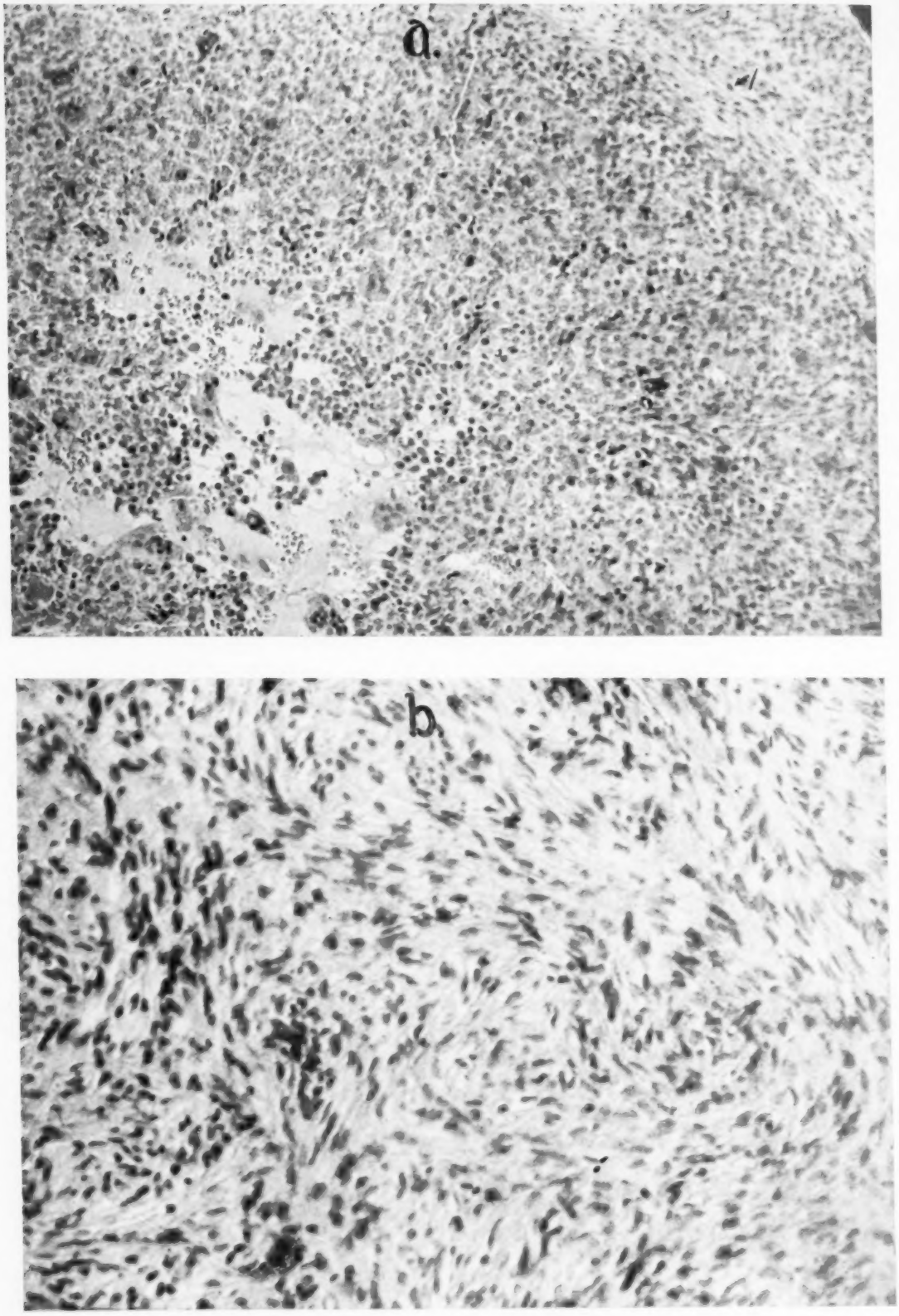

FIG. 7. Case II. (*a*) Photomicrograph (low magnification) of biopsy material. Very cellular giant-cell tumor with markedly cellular stroma; many spindle cells; giant cells small; tumor showed an attempt at encapsulation (1).

(*b*) Higher magnification of more central area showing whorls of spindle cells with hyperchromatic nuclei varying greatly in size and staining reaction; apparent malignant change in giant-cell tumor stroma.

fields, and on December 10 and 12 over the posterior right and left lung fields.

The patient went home on December 25, walking on crutches, with little pain and much stronger. He was to return January 19, 1931, but was reported by his physician as too ill to travel in the winter weather. We have a report of June, 1931, that the patient was still alive, weak, but in little discomfort.

This case presents, we admit, only presumptive roentgen evidence of metastasis to the lungs. It offers, perhaps, an example of the inadequate early treatment of the giant-cell tumor—and the possibility of exacerbation—probable malignant degeneration and metastasis. This would appear the result of repeated insult to the original lesion, rather than the constitutional damage from hemorrhage or secondary infection in the neoplasm, as is commonly discussed in the older literature. The metastases, as we consider the pulmonary lesions to be, may not be giant cell tumors—perhaps round or spindle cell sarcoma, or even osteogenic sarcoma. And yet it is conceivable that repeated trauma or the close proximity of giant-cell mass and thin-walled vascular channels might permit of tumor cell emboli, as was suggested by Stone and Ewing.

So much for the roentgen and histologic identification of the giant-cell bone tumor, a benign lesion of the skeletal architecture, very frequently alleged by the patient to arise as a result of minor or major trauma to bone, and which may, under certain circumstances, serve as a source for a general malignancy, probably of a much less well-differentiated cell type.

(*c*) Response to Treatment.

We come then in such a problem in natural history to the consideration of the response of the neoplasm to its environment.

From Paré to the present, there has been the advice on the part of the considerate and conservative surgeon to curette or excise the area of the tumor. There has also been on the part of some the further caution that recurrence is to be anticipated unless curettage is accompanied by chemical cauterization.

The mechanical nature of the lesion should readily confirm at least the latter. A multilocular, proliferative lesion could easily have one or more small masses of giant cells left intact in the process of curettage, more often than not, whence the neoplasm may regrow, unless some means of growth restraint or even lethal insult is administered to all possible remnants of the tumor.

Reference to Table 1 of clinically cured cases—and to practically all the several groups of collected cases in the literature—will show evidence of more rapid and complete healing when a chemical cauterant accompanies the surgical excision (Cases No. 133387, 142767, 154956, 222289). This is particularly true if we are to consider seriously the factor of greater growth capacity in the younger individual.

From the cosmetic standpoint, surgical intervention, with cauterization, is probably advisable in all cases where visible deformity impends. This of course presumes an accessibility of the neoplasm greater than the potential damage to the patient by the intervention. Such a consideration pertains from the functional standpoint as well.

On the other hand, the surgical approach offers a certain general risk, a period of disability, and the possible local risk of secondary infection, of hemorrhage, or both. Consequently, if some other means of growth restraint can be offered which does not necessitate these risks, the patient and physician both gain. Further, if there is any possible confusion in diagnosis between giant-cell bone tumor and the malignant neoplasms, surgical approach to the latter in the skeleton has not been shown to be a method of choice, even in the radical disarticulation of a whole extremity.

In the opinion of Ewing, Herendeen, and others, roentgen irradiation offers a means of definite growth restraint in giant-cell bone tumor without the risks referred to above. Of course, in those cases in which weight-bearing may engender "pathologic"

fracture in the tumor area of an extremity, adequate prophylactic supportive measures are necessary. By roentgen therapy is not meant one, or two, or three unrelated treatments with such an agent, but a carefully planned, progressive program. This requires time, patience, and cooperation. When surgical intervention seems imperative from the cosmetic or functional standpoint it is our opinion that, unless adequate excision of a part, such as the fibular head, is undertaken, curettage and cauterization should be followed immediately and persistently by roentgen therapy. We are not yet ready to commit ourselves on the advisability in such cases of preoperative irradiation, partly because of the difficulty of restraint of the surgeon for an adequate period after institution of irradiation.

It is of interest to note that of the 10 cases in our series considered as cured 5 have responded satisfactorily to irradiation alone; 3 had curettage, cauterization, and irradiation; one irradiation, curettage, cauterization, and irradiation, and one excision. In 3 of the first 5 (Nos. 124352, 135259, and 261179) the cosmetic result was better than could have been obtained with surgery—in one (No. 184471) surgery beyond biopsy would have probably been disastrous—and in the other (No. 213022) surgery had been attempted previously without benefit.

On the other hand, Case No. 142767, with cauterization, phenolization, and irradiation probably had the most perfect anatomical restoration. Such is possible in the growth period of the younger individual.

If we consider the cases in Group II, "Recurrences," one immediately is struck by the sad results of imperfect liaison between patient, surgeon, and roentgenologist whereby there has been possible only sporadic irradiation. Or, perhaps, panic has influenced premature surgical intervention in the reactionary phase of the bone after institution of irradiation; simple curettage and fracture of the cortex into the gap thus produced, without cauterization or proper consistent therapy, has been effected. The usual result then is either further surgery, even to excision and perhaps permanent disability, or the almost impossible task of trying to inhibit the growth by further irradiation.

As a case in point, demonstrating the problem of irregularity in program and of the effect of irradiation, attention is called to the following:

Case III (No. 246845). White, male, farmer, aged twenty-two. Admitted August 13, 1930, with history of stiffness of left knee beginning in October, 1929. Gradual increase in size of upper inner leg at knee. Roentgen examination elsewhere, March, 1930, said to have been reported negative. Roentgen examination August 11, 1930, elsewhere, showed a lobulated expansile tumor of the tibia extending from the under surface of medial articulating plateau downward for 3 inches (Fig. 8*a*).

Examination August 13, 1930, showed definite tumefaction of the leg, some increase in temperature, tenderness on pressure with definite "eggshell crackling"; no adenopathy; Kahn test negative.

Clinical and roentgen diagnosis: Giant-cell bone tumor.

Roentgen therapy advised and started August 14, 1930: 120 kv. peak, 30 cm. focus skin distance, 4.0 mm. Al, 150 r, anterior tibia. This was repeated on August 15, total 450 r, and the patient was instructed to return on September 15. At that time (Sept. 15) he reported total loss of pain; the tumefaction was slightly more prominent than before. Another 150 r of the same quality was administered. Roentgen examination on September 19, 1930, showed increase in bone lysis, periosteal proliferation, loss of sharp cortical differentiation (Fig. 8*b*). Surgical consultation raised doubt of benign character.

September 25, 1930, surgical intervention with curettage of a very vascular tumor—thin plate of cortical bone described. The cavity was filled with bone chips from the lower tibial crest; no cauterization; wound closed. Postoperative condition on October 3 shown in Figure 9*a*. Some regeneration of cortical bone, some peripheral calcification in trabeculae.

Re-examination by roentgen ray on October 7, 1930, January 6, 1931, and February 11,

Fig. 8. Case III (246845). (*a*) August 11, 1930. Films brought by patient. Large rarefaction in head of tibia, anteromedial, fine trabeculations; giant-cell bone tumor.

(*b*) September 19, 1930. One month after first series of roentgen therapy. Apparent gross lysis of bone in tumor area; loss of trabeculations; slight depression of medial tibial plateau.

1931, showed no evidence of incorporation of bone chips in a bone regenerative process. On February 11, 1931, attention of the surgeon was called to an increase in rarefaction at the lower end of the excavated area suggesting regrowth of the neoplasm, apparently downward into the surgical defect (Fig. 9*b*).

June 22, 1931, re-examination by roentgen ray demonstrated rather gross lysis of the bone chips and positive absorption of bone from the shaft (Fig. 10*a*). The pain was returning. The surgeons were urged by the Department of Roentgenology to return the patient for resumption of therapy (nine months after withdrawal for surgical intervention). Roentgen therapy was resumed June 24, 1931.

More active and radical therapy was deemed advisable than before. The patient received treatment as follows:

Date	kv. peak	FSD cm.	mm. Al	Dose	Area Left tibia
June 24	120	30	4.0	450 r	ant. head
June 27	120	30	4.0	450 r	med. head
July 2	120	30	4.0	450 r	lat. head
July 10	140	30	4.0	500 r	ant. head
July 17	140	30	4.0	500 r	med. head
July 24	140	30	4.0	350 r	lat. head

Roentgen examination September 4, 1931, showed again the bone lysis previously observed after irradiation (Fig. 10*b*), but the patient no longer complained of pain, and the mass was no larger.

Histopathology. Sections removed at the time of surgical intervention September 25, 1930, demonstrated a giant-cell tumor with enormous numbers of very large giant cells of the epuloid type, very cellular and very vascular, dilatation of the small blood vessels, areas of extensive necrosis with hemorrhage. In these latter and bordering them were giant cells in which the nuclei were shrunken, matted together, some disintegrated with much chromatin dust, other giant cells with vacuolated protoplasm. These characteristics are well shown in the photomicrographs (Figs. 11 and 12).

In our opinion, this case presents rather well the changes to be anticipated immediately after irradiation—bone lysis, increased vascularity, internal necrosis with hemorrhage. This reaction does not begin to subside for a month to six weeks. Our observations coincide with those of Herendeen. Recalcification is seen by the end of a two-month period, and normally goes progressively forward from that time. It is during this two-month interval that the physician may become somewhat apprehensive over the apparent growth and destruction from the neoplasm, and be influenced thereby, with resultant (in our opinion) premature surgical intervention.

Once this latter has occurred, and the patient is not promptly returned to the roentgenologist for further treatment, one may anticipate the problem which this patient now presents, demonstrating perhaps the futility of the attempt of the radiologist to catch up with the neoplasm after a lapse of time following the surgical interference.

It is too early in this case to determine exactly how much we may hope to accomplish. It may be necessary to resort to amputation to permit the best function. He may present a malignant lesion, in which case nothing of value can be done. He is to return in a month, at which time we hope to be able to see some progressive repair.

Roentgen Therapy Program. Reference to Table v giving therapeutic procedure in detail of all except the 3 cases considered above will at once call attention to the separation of these cases into two general groups—one being treated with roentgen radiation produced at 120–140 kv. peak, the other with that produced at 200 kv. peak. Recurrent changes in personnel of the section on therapy during the period covered by this series has contributed to a fragmentation of any consistent program. However, in general, the procedure has been one of conservative therapy—relatively larger single, or smaller multiple exposures during the first weeks or months, gradually shading off as the bone production increases and the tumor decreases. The two voltage values are utilized with the idea chiefly of using as long wave length as is compatible with economy of time and effect—the lesser value for the case with

Fig. 9. Case III. (*a*) October 6, 1930. Seven weeks after initial radiation therapy, eleven days after surgical intervention by curettage and emplacement of bone chips from lower tibial crest. Recalcification of cortical bone and in peripheral trabeculae after irradiation.

(*b*) February 9, 1931. Further recalcification of the cortical bone, but apparent resumption of bone lysis (probably by tumor) in lower and lateral portion of curetted area. Medial tibial plateau firm.

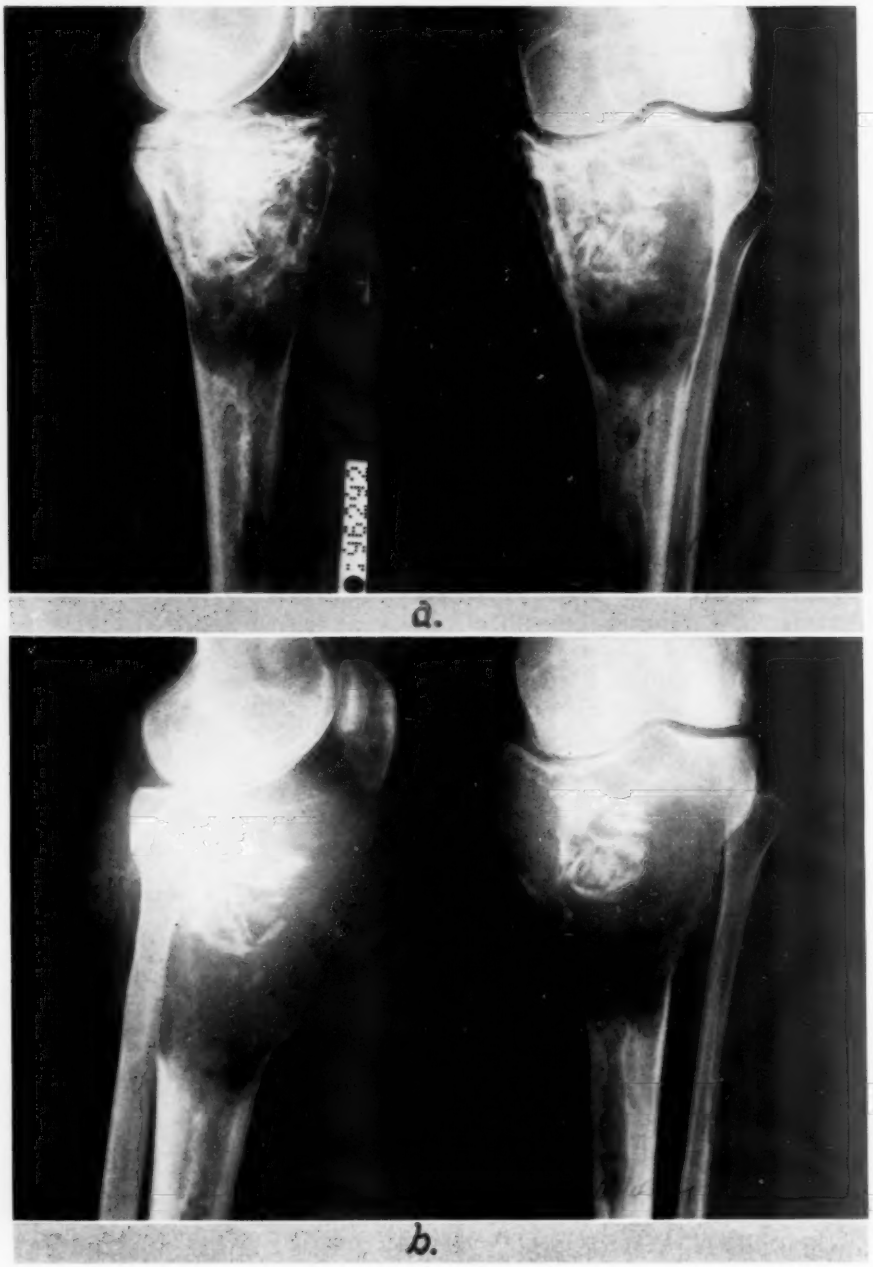

Fig. 10. Case III. (*a*) June 22, 1931. Continued ossification of cortex and subcortical area, but marked destruction of bone chips and apparent destruction of medullary portion of tibial crest along source of bone chips. (No roentgen therapy since September, 1930.) Recurrence of giant-cell bone tumor.

(*b*) September 4, 1931. Sharp reaction two months following resumption of roentgen therapy. Prognosis not very favorable although the destruction in lower tibial crest seems retarded.

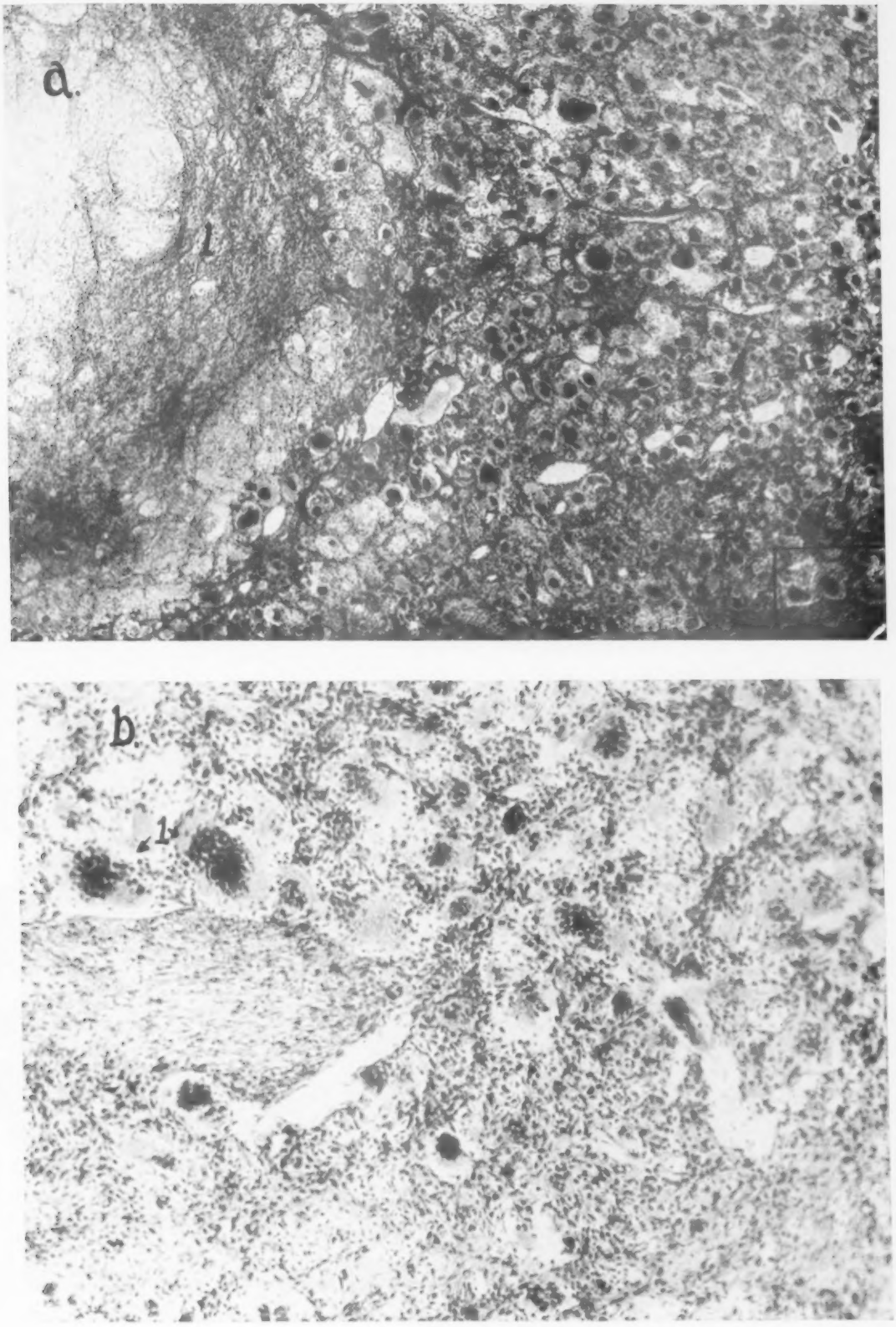

FIG. 11. Case III. (*a*) Photomicrograph of tissue removed September 25, 1930, five weeks after initial roentgen therapy. Large necrotic area on left (1) with much chromatin dust. Neighboring areas show large vascular channels (2), large giant cells with marked clumping of nuclei, many spaces showing remnants of giant cells.

(*b*) Higher magnification. Detail from area partially shown in lower right corner of (*a*). Typical bone tumor giant cells (1) with large amount of cytoplasm, central multiple nuclei; stroma quite cellular.

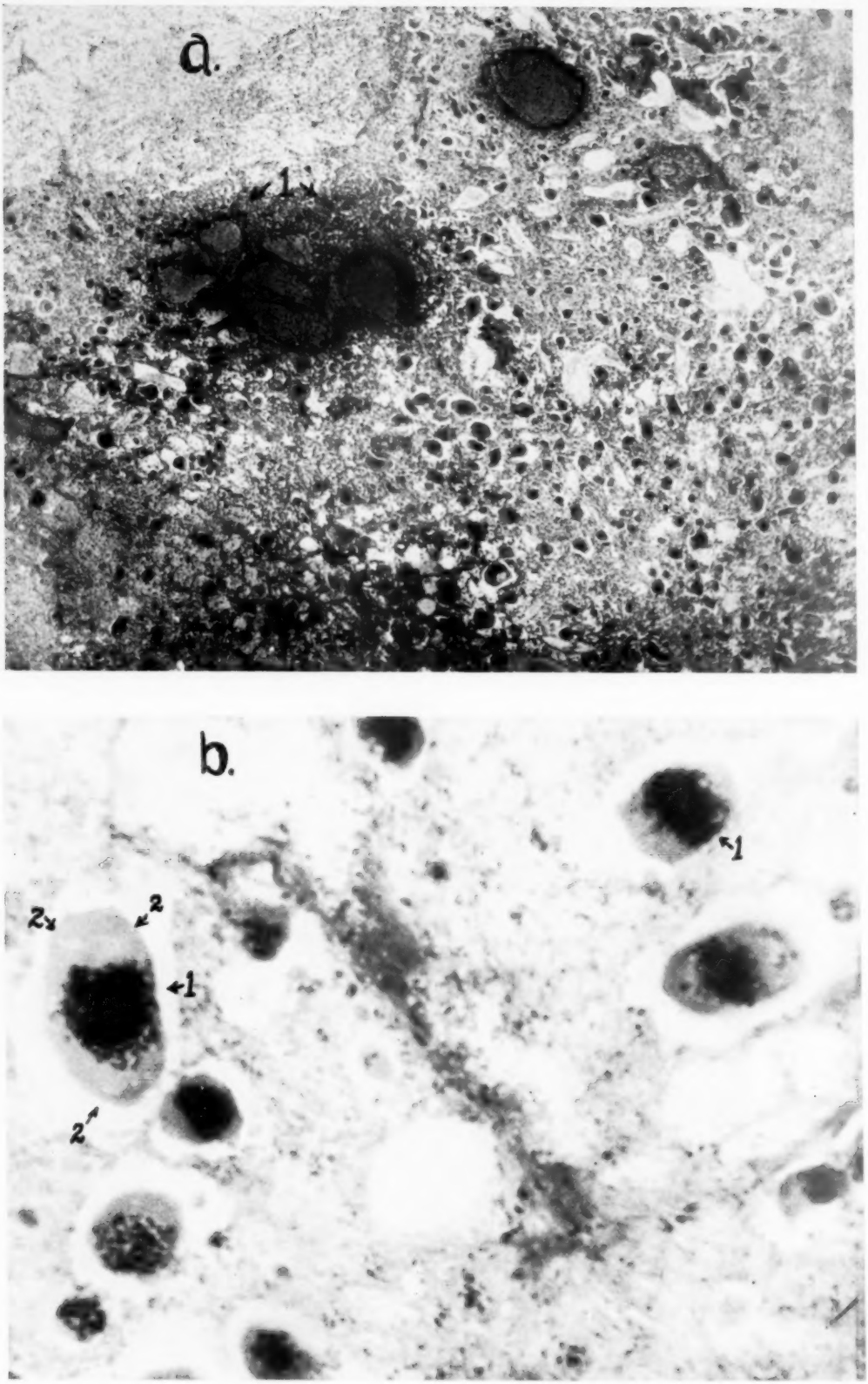

FIG. 12. Case III. (*a*) Photomicrograph of tissue removed five weeks after roentgen therapy. Considerable hemorrhage into stroma about the large vascular spaces (1). Giant cells show rather marked clumping and pycnosis of nuclei; many apparently disintegrated leaving chromatin dust in cytoplasm and scattered through the stroma.

(*b*) High power magnification showing marked clumping of nuclei in the giant cells (1); pycnosis and vacuolization of the cytoplasm (2) suggesting death of the tumor cell. Dark particles in the stroma are largely chromatin dust.

thinner overlying tissue, the greater for heavy parts as spine and femur. The reaction shown compares closely with the experience at the Memorial Hospital, New York City.

The major intent in roentgen irradiation of giant-cell bone tumor should be that of growth restraint, and no more. I am somewhat doubtful, as I review these cases, of there being an appreciable value in delivery of lethal doses of roentgen radiation. Those cases in which relatively moderate or mild doses were given and frequently repeated seem to have produced the best results.

Further, attention is again invited to the relatively less favorable response after intervention by surgical means. This is especially true after a non-cauterization at the time of the surgical approach. Once intervention has occurred, the patient should be referred to the roentgenologist, and roentgen irradiation immediately resumed.

SUMMARY

1. Nineteen cases of giant-cell tumor, 14 confirmed by histopathologic study, are analyzed—10 considered clinically cured, 2 presenting malignant features.

2. No evidence has been found to refute in general the customary belief that giant-cell bone tumor is essentially benign, suggestively neoplastic rather than inflammatory. Although in the presence of evidence of alleged pre-incident trauma and of possible intraosseous hemorrhage, the consideration of an etiology in reparative or reactive granulation tissue must be weighed heavily against the neoplastic idea. In this regard Robin's original delineation is interesting as proposing an undue proliferation of an ordinarily normal, although sparse, constituent bone medulla cell.

3. It is a disease of the metaphysis; the epiphysis as such is not involved. Wherever the neoplasm occurs after the epiphyseal disc has been obliterated by ossification, the tumor may invade to the under surface of the articulating cartilage.

The various types of giant cell tumor are not consistently differentiated by roentgenographic methods.

4. The conception of treatment with intent of growth restraint is very important. Roentgen irradiation in repeated relatively moderate doses offers the most for the patient, except when for cosmetic or functional reasons better results could be obtained with the addition of surgical intervention.

5. Surgical intervention should not follow roentgen therapy short of six weeks to two months.

6. If surgery is contemplated, thorough curettage and equally thorough chemical cauterization of the cavity should be executed, followed immediately by a consistent roentgen therapy program.

7. Surgery without cautery or immediate roentgen therapy has not offered so satisfactory a result in most cases.

8. Malignant degeneration of part of a giant-cell bone tumor, or concurrent origin of a malignant neoplasm is believed to be shown in 2 cases—one without peripheral metastases, one with pulmonary metastases. In the latter, the lung involvement might be the result of giant-cell emboli from the original gross tumor. With this in view, the less the neoplasm is disturbed by trauma, accidental or induced, the less likely will there ensue a proliferative response of uncontrolled character.

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DISCUSSION ON PAPERS OF DRS. KIRKLIN AND MOORE, PFAHLER, AND PEIRCE

Dr. A. H. Pirie, Montreal, Canada. Dr. Kirklin emphasized the two types that we have of this disease, the classical one in which the trabeculae are well formed, and the one in which fusion takes place. We are more accustomed to the classical which I have always called the "tennis racket." I have seen it for many years. But the diffuse form is not so common. Is the one a type of the other, or is it due to some other cause? For instance, the classical one is seen at the lower end of the radius. Is it seen as often at the lower end of the femur? There is no pressure brought to bear on the lower end of the radius and there is continual pressure on the lower end of the femur. Has that anything to do with why we get the two different types? Whether it has or not, or whether the one leads into the other is a difficult question to decide. I have watched the classical one for a long time and not seen it develop into the fused form.

Dr. Pfahler's long experience in this and his very valuable slides which he has shown us are extremely interesting. One thing which he brought out is the fact that if we can make a good diagnosis, a fairly sure diagnosis of giant-cell sarcoma, should we really call in a surgeon and ask him to confirm our diagnosis, or should we not? I think we should not if we can make a certain diagnosis that it is giant-cell sarcoma. We should not ask the surgeon to come in and operate, because consider what happens in a case of fracture. When a fracture takes place in bone sarcoma it does not help the healing of the sarcoma, and an operation, or biopsy by the surgeon does not help it either. Then if we make a mistake and it turns out to be a malignant osteogenic sarcoma, how much harm have we done the patient? Do we not by intensive roentgen treatment tend to prevent metastases? I have seen such a case in which there was a malignant sarcoma of the lower end of the femur. It was given intense roentgen therapy for a year and a half and then the leg was amputated. The patient did not develop metastases, even after that long period of time. So it is possible that even although we do not do any good, we don't do any harm in such a case as that.

Dr. Peirce showed us some beautiful pathological slides and one case especially in which spindle-cell sarcoma was dotted over with giant-cell sarcoma. I have a similar case in which very intense radiation went on for years and no metastasis took place, and that patient is now clinically cured.

The two principal points, then, I wish to make are the types, the fused and the classical, and the third point is, do not call in a surgeon unless it is absolutely necessary.

Dr. Ralph S. Bromer, Philadelphia. My experience in the radiation treatment of giant-

cell tumors has been very limited. From the point of view of diagnosis, Dr. Kirklin has done a great service in classifying these types.

Geschickter's work on giant-cell tumors has been of great assistance in the differential diagnosis. Transitional or variant types exist which may be really various stages of growth of the giant-cell tumor process. Thus he has described the giant-cell variant of the bone cyst and the spindle-cell variant of the giant-cell tumor. In the former, slides may show typical chronic cystic osteitis and others from the same lesion may show an appearance of giant-cell tumor. In the second instance, slides may show typical giant-cell tumors and others spindle-cell sarcoma. So it is impossible at times in these "variant" lesions, to make a definite diagnosis and to distinguish between a benign giant-cell tumor and an osteogenic sarcoma.

DR. RALPH E. HERENDEEN, New York City. Drs. Kirklin and Moore have shown that some giant-cell tumors are accompanied by rapid destruction of bone. This tumor differs in its roentgen features from the typical or textbook type of giant-cell tumor which is usually so easy to diagnose and differentiate from other bone tumors.

The variations in the roentgen features of giant-cell tumors are frequently the result of the rate of growth. Those of slow growth which are accompanied by an attempt at repair and limitation give rise to the clean-cut trabeculated tumors which grow equally in all directions, and are more or less limited in progress up the medullary portion of the bone. These are therefore distinctly different in their roentgen appearances from the rapidly growing, cellular giant-cell tumors which destroy bone readily and therefore grow in an irregular manner and do not present the multicystic trabeculated appearance which characterizes the tumors of slow growth.

Would it not be well, therefore, to bear in mind, when classifying the various types of giant-cell tumors, that the rate of growth plays an important part in the production of the clinical picture and roentgen appearance.

Frequently, after roentgen therapy, these rapidly growing giant-cell tumors, which may simulate in the roentgenograms osteogenic sarcomas or metastases from carcinoma, take on the more characteristic features of the typical benign giant-cell tumor. The roentgen ray, therefore, may be employed therapeutically sometimes as a diagnostic agent in the differentiation of bone tumors.

It is very gratifying to know that roentgenologists generally accept roentgen therapy as the method of choice in the treatment of giant-cell tumors. It is to be deplored that many of our surgical friends have not as yet come to that view with us. Amputations are still performed, curettements done for recurrences which might be obviated through the employment of roentgen therapy.

Most of our failures in the roentgen therapy of giant-cells tumors have been in the treatment of recurrences. It is very uncommon to fail to obtain a satisfactory result in the roentgen treatment of primary giant-cell tumors, or where no other treatment has been employed prior to the institution of roentgen therapy.

Recurrences of giant-cell tumors following curettage in the upper end of the tibia are not infrequent, and in many instances where these tumors became transformed into malignant processes which metastasized to the lungs and caused the death of the patient, a large proportion of them were giant-cell tumors in the upper end of the tibia.

DR. JAMES EWING, New York City. It is very gratifying to see that roentgenology at least is reaching definite, and I think sound, conclusions regarding the main points of giant-cell tumor, owing to the original observation of Dr. Pfahler, which I am very glad he emphasizes, and which we all recognize, and to the services of a great many roentgenologists and some pathologists.

As the material increases and our curiosity expands and we attempt to ask questions about the origin of this group of tumors, to my mind, the subject is becoming more complex rather than more simple.

I would like to ask the attention of roentgenologists to some clinical questions concerning giant-cell tumors, for it is obvious that they do not all arise under the same conditions. I have an impression that the conditions of origin determine very largely the course of the disease, and the various roentgenological differences which you have been discussing. It seems clear that some tumors arise as a result of some disturbance, possibly hemorrhage, in the cortex of the bone. Under those circumstances they are very apt to be active and much bone is produced. Diagnosis is difficult and some pathologists regard them as osteogenic sar-

comas. Some of them are reported as spindle-cell sarcomas mixed with giant cells.

In another group the disease is often multiple. These are unquestionably related to osteitis fibrosa cystica, sometimes associated with tumors of the parathyroid, and here we have the simple more benign characteristic types of giant-cell tumors. There are others which I think are the result of the absorption of misplaced islands of cartilage, probably as a sequel of old rickets or some other disturbance in the structure of the bone at the epiphyseal line. These give rise to a good many differences of opinion, both roentgenologically and from the pathological side.

There are a few tumors which it seems to me must be referred to as true connective tissue growths in the marrow, with or without myxomatous and chondromatous features. These may be associated with many giant cells and they give a different roentgenologic and histological picture and therapeutic course. There are probably other clinical conditions under which these giant-cell tumors arise, and since it seems probable and most fortunate that in the future the care of giant-cell tumors will be mainly in the hands of the roentgenologists, I trust they will not feel that their responsibilities do not cover the thorough clinical and pathological investigation of these conditions of origin which I think are the real questions that face you.

I wish to support in every particular the authoritative advice of Dr. Pirie that the surgeon should not be called in to treat these cases. I have seen so many bad results from recurrence, malignant transformation, infection of all types, acute and chronic, resulting in amputation, that I have no longer any room to file these cases in our museum. The reports that we get from the surgical side of excellent results from surgical treatment I think do not do great credit to the frankness of our surgical friends.

At the present time the prognosis for a patient with giant-cell tumor in this country is comparatively unfavorable, owing to the unfortunate results of surgical interference. This at least is my experience. At the same time I wish to caution the roentgenologist who has not had a very large experience in this field that there are certain types of giant-cell tumor that do not respond well to radiation. Some of the very large tumors are difficult to handle on account of their bulk. Absorption after destruction is not possible with the conditions of the circulation, and while you may destroy the whole tumor, you do not get healing. Some amputations are necessitated by that factor. There is a type of very vascular giant-cell tumor, almost like an angioma with giant-cell tissues around the distended sinuses, not much described in the literature, but not at all infrequent. Some of these tumors pulsate; most of them do not. They do not do particularly well with irradiation and generally terminate in amputation.

There is also that group, of course, which is malignant from the first. There are in the Codman register three or four cases of this sort, and I have seen in recent years others which have not been recorded, where from the very beginning a definite destructive process, invasive, quite different from ordinary giant-cell tumor, occurs, associated with a structure which shows spindle cells, which any pathologist would regard as malignant. These metastasize and kill. That type of tumor must be recognized by both surgeon and roentgenologist.

So the subject, it seems to me, expands in difficulty and in importance as our knowledge increases.

Dr. John S. Derr, Frederick, Md. Dr. Kirklin and Dr. Pfahler have described cases of giant-cell tumor characterized by absence of the bone striae in the tumor mass. My excuse for imposing on your time is to report a case which has been under my observation for sixteen months. This showed complete destruction of bone without striae.

It was characterized by four things that are interesting: entire lack of swelling of the soft tissues, rapid growth, recalcification under high voltage roentgen therapy and failure to metastasize in the chest or anywhere else. This girl is now what we would call clinically well as far as I can observe. The case came to me for roentgen examination suffering with pain in the knee and hip and a marked limp. She at that time had a secondary anemia. The first slide shows a complete destruction of the right pubic bone. Dr. George B. Bennett of Baltimore was called in consultation at once in this case and pronounced it osteolytic sarcoma and refused to do a biopsy, recommending high voltage roentgen treatment.

Second slide. This was taken four months after a dose of eleven hours of high voltage, 200 kv. treatment, 0.75 mm. Cu filter, given over 20 cm. areas front and back, 30 minutes to the dose. The idea of the divided dosage was to re-

duce the roentgen sickness to which she was very susceptible. You see here the head of the femur appears to be going into the pelvis. The ischium is destroyed and part of the ilium here.

Third slide. At that time these slides were shown at Dr. Bloodgood's clinic and he and Dr. Geschickter pronounced it osteosarcoma. The patient was very ill at the time but gradually improved. This slide shows a regeneration of bone taking place in the pubes, ischium and ilium, but the head of the femur has gone further into the pelvis and is almost resting on the ilium.

Fourth slide. In about two months more the patient had markedly improved clinically. You see a further recalcification. Now the ilium is practically resting on the trochanter major. At this time she was having no pain and was feeling well.

Fifth slide. This was last February. At this time the patient was able to ride in an automobile and go swimming; she was comfortable at all times. The last examination made in September of this year showed calcification throughout to be more dense. What the final result will be, we of course do not know, but there was no swelling of the soft tissues whatever, the bone has healed and the skin is in good condition after fourteen hours of high voltage roentgen therapy, and the patient has gained over 20 pounds in weight.

Dr. Kirklin (closing). I wish to make it clear that we do not claim any originality in recognizing this second type of giant-cell tumor as similar cases have previously been reported, but in view of the fact that almost half of our cases are of this type we felt that it was worth calling attention to. We have not observed a single case of giant-cell tumor which had undergone malignant degeneration.

Dr. Pfahler (closing). I would simply like to remark upon two things. In the first place, I am very glad that Dr. Pirie and Dr. Ewing agree that the surgeon should not interfere except in special cases where a conference has decided that it is advisable. Secondly, I believe that the rate of recovery depends in part upon the rate of development of this tumor. A slowly developing tumor will probably repair more slowly than one that has developed more rapidly. Therefore, the history of these cases is probably very important, as has been emphasized by Dr. Ewing, and we should continue, as he has suggested, to gather all the data possible with regard to this class of tumors. Thirdly, I do believe that it is possible for these cases to become malignant or that there is a malignant element in them which therapeutically we destroy, or in other instances additional traumatism from the surgeon may stir up the malignant cells in them and we get metastasis.

Dr. Peirce (closing). I appreciate very much the comment of the discussants. We wish to leave with you this observation, confirmed by a major number of essayists, that the prognosis of response is much poorer after inadequate prior surgical intervention and possibly inadequate therapy, or, in the case of which Dr. Ewing speaks, with the type which does not respond readily to roentgen therapy. We prefer to have the patient for roentgen therapy alone without prior damage from one cause or another.

Secondly, in the matter of interruption of roentgen therapy, the third case which I presented, the young boy, presents certain features of that problem; namely, the difficulties attendant upon the interruption of a program of treatment for the case, the intervention by the surgeon prematurely, and then no return to the roentgenologist for about nine months.

OSTEOPOROSIS CIRCUMSCRIPTA OF THE SKULL AS A FORM OF OSTEITIS DEFORMANS*

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INTRODUCTION

THE disease "osteitis deformans" was first described in 1876 by Sir James Paget in a paper entitled "On a form of Chronic Inflammation of Bones." In this communication he reported 5 cases with the post-mortem findings of 2 (Cases 1 and 4). In a second paper 3 more cases were reported and it is worthy of note that 5 of his 8 cases ultimately died of malignancy arising in the osseous structures. Since then an abundance of literature has appeared on the subject which consists for the most part of case reports, but few important facts have been added to Paget's original description of the disease.

Schüller used the term "circumscribed osteoporosis" for the first time in his article in the *British Journal of Radiology* in 1926 to describe a condition of the skull in which a large part of the anterior half of the calvarium was transparent, and had sharply defined irregular borders. He commented that he was unable to say anything regarding the etiology of the condition.

LITERATURE

The belief that osteoporosis circumscripta and Paget's disease are one and the same disease was suggested by Sosman in 1926, Schüller in 1929 and Weiss in 1930. In 1927 Sosman recorded a case of osteoporosis circumscripta of the skull on which a biopsy had been done and the pathological report revealed simultaneous proliferation and degeneration of the bone with complete absence of the Haversian system, a picture similar to that found in Paget's disease. The findings were considered those of an atypical form of osteitis deformans.

In 1927, Whitlock reported a case in which the skull changes bore a close resemblance to those of our first case. His patient had a tumor of the jaw in the right upper molar region. The roentgenogram disclosed a mass infiltrating the orbits and accessory sinuses. There were extensive lesions in the skull and the microscopic examination of a section from the growth of the upper jaw resulted in a diagnosis of adamantinoma. However, no histological sections of the cranial bones were made.

In April, 1929, in the *Medizinische Klinik*, Schüller reviewed the literature and briefly described 5 cases. In this article he again declined to make a definite statement regarding the nature of the disease, although he suggested that there might be a relationship between Paget's disease, osteoporosis circumscripta, and cachectic osteomalacia. He also stated that the first case reviewed in his article had a questionable sarcoma of the skin.

In 1930, Weiss presented 2 cases of osteoporosis circumscripta of the calvarium. Both patients had typical Paget's disease in other parts of the skeleton. His second case was followed for a period of about three years during which time there was not the slightest degree of transition or evolution into Paget's disease. He noticed, however, that the osteoporotic area of the occipital bone had gradually increased in size. He raised the question as to whether these changes could be the first manifestation of osteitis deformans and concluded that osteoporosis circumscripta is not a transitional form of Paget's disease but is an independent and rare manifestation of it.

In the same year Meyer-Borstel reported 3 cases of osteoporosis circumscripta of the skull with Paget's disease in other parts of the skeletal system.

It is not within the province of this paper to discuss the etiology and symptoma-

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tology of osteitis deformans, for these have been described many times in the literature. (See especially the articles by Paget, Moore, Taylor, and Hirsch.) Nevertheless, we would like to quote a few paragraphs from Paget's classical description of the pathology of osteitis deformans, so that the roentgenological changes may be more readily understood. He states:

The whole microscopical architecture of the bone has been altered; the structure appears to have been almost entirely removed and laid down afresh on a different plan and in a larger mold. . . . The sides of the widened canals instead of being smooth and even, are eaten out in a series of curves and concavities with the production of Howship's lacunae so characteristic of inflammation. The tissue contained in the canals, too, almost precisely resembles the tissue found in the spaces of inflamed bones only differing from it in being generally more fibrillar and less rich in cells, a fact easily to be

Fig. 1. A reproduction from Paget's original article showing that Paget's disease involves mainly the outer table and diploë. Note the compact area in the diploë at *A*, which would be shown on a roentgenogram as a round, dense shadow.

Fig. 2. Case 1. Lateral view of the skull showing a large osteoporotic area in the frontal, parietal and temporal bones. This film was taken in 1922.

accounted for by the very long duration of the disease and the general tendency towards organization which was displayed throughout.

The modern conception of the pathology is essentially similar to that which has been quoted above.

Paget's disease of the skull usually presents a fairly typical and well-known roentgenographic appearance. In brief, it consists of a thickening of the bones of the skull with coarse mottling throughout the calvarium due to alternating areas of increased and diminished density. In addition, the trabeculae are coarse and prominent. To this description we would add the further observation that the outer table and diploë of the skull are the portions of the bone which are first to be involved and which show the most pronounced lesions (Fig. 1).

CASE REPORTS

It is our purpose to present 12 cases of osteoporosis circumscripta with particular reference to the roentgenographic findings in the skull.

Case 1. Hospital No. N.I. 2304. J. M., a white woman, aged sixty-eight, was admitted to the Neurological Institute January 16, 1930, because of chronic alcoholism. The physical examination revealed no evidence of organic disease. The laboratory tests including serology,

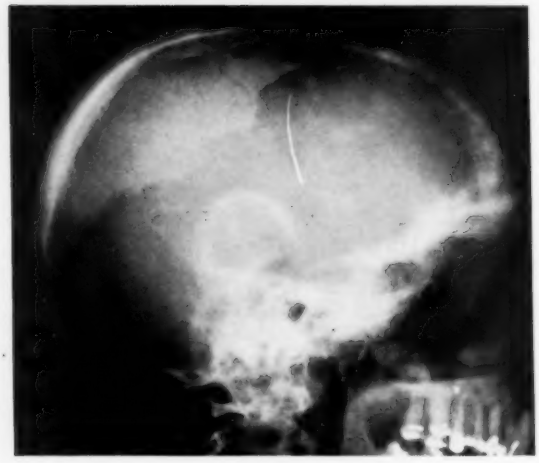

Fig. 3. Case I. Lateral view of the skull, taken in 1930, showing the changes which have occurred at the end of an eight-year interval. Note the areas of increased density and the thickening of the frontal bone; also the increase in density of the bones at the base and the spread of the disease.

blood culture, urinalysis and blood chemistry were negative. The patient was discharged from the hospital two weeks after her admission. She died several months following her discharge.

A film of the skull which had been taken by Dr. F. H. Baetjer in December, 1922, showed an extensive area of decreased density in both fronto-parietal regions but no thickening of the bone (Fig. 2). Our films, taken January 20, 1930, show a definite increase in the extent of the lesion. In addition there is a distinct thickening of the frontal bone which was not present in the previous film. Furthermore, rounded areas of increased density are now present in the involved area and the bones of the base are denser than normal and the trabeculae appear exaggerated, as is seen in typical Paget's disease of the skull (Fig. 3).

This case demonstrates that the disease progresses very slowly, and it shows the transition of osteoporosis circumscripta into Paget's disease.

Case II. Hospital No. N.I. 4805. P. B., male, Hebrew, aged seventy, was admitted to the hospital May 5, 1930, complaining of lancinating pains over the left side of the face for the past ten years. He had received a number of alcohol injections into the fifth nerve. The physical examination revealed advanced arteriosclerosis, emphysema and an enlarged prostate gland. The laboratory findings, including the Wassermann test, were negative. A diagnosis of trigeminal neuralgia was made. He was discharged from the hospital on May 21, 1930, and died July 1, 1930.

Roentgenological examination of the skull on May 7, 1930, revealed an extensive thinning of the occipital and parietal bones (Figs. 4 and 5). The involvement of the outer table and diploë by the disease and the relatively intact inner table are well demonstrated in this case.

Case III. Hospital No. N.I. 8830. S. G., female, aged thirty-two, entered the hospital June 5, 1931, complaining of pain in the head and inability to concentrate. In 1924 the patient had been knocked unconscious by a blow on the head from an iron door. On recovering consciousness she was unable to speak for about twenty minutes and a few days later for a short time she complained of paresthesia of the upper extremities. No evidence of organic disease was found. The final diagnosis was traumatic neurosis.

The roentgenograms of the skull showed a large circumscribed area of decreased density involving both parietal bones and the occipital bone above the torcular Herophili (Figs. 6 and 7).

This patient had a skull trauma seven years prior to her admission, but in our opinion this injury was of no significance in the development of the osteoporotic lesion.

Fig. 4. Case II. Lateral view of the skull showing marked and diffuse thinning and decalcification of the parietal and occipital bones.

Fig. 5. Case II. Anteroposterior view of the skull showing the bevelling of the bone in the upper parietal region, bilaterally. Only the outer table and diploë are involved.

Fig. 6. Case III. Anteroposterior view of the skull showing a large circumscribed defect in the occipital and posterior portion of the parietal bones.

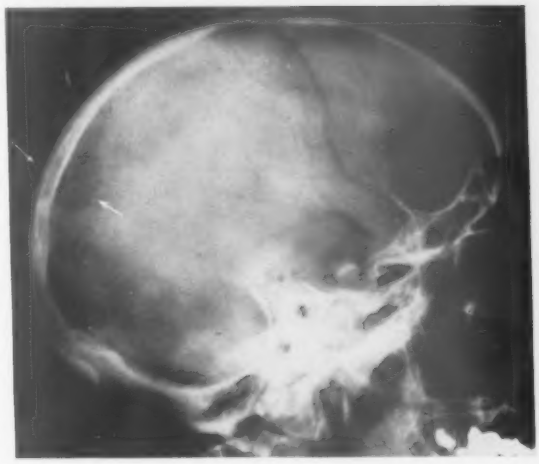

Fig. 7. Case III. Lateral view of the skull to show the position of the lesion.

Case IV. Hospital No. N.I. 8632. W. P., a jeweler, aged thirty-six, entered the hospital in April, 1926, with a recent history of temporary semi-conscious state, occasional vomiting, diplopia and drowsiness. The neurological examination was essentially negative.

He was readmitted to the hospital in August, 1931, complaining of the same symptoms as on the previous entry. The physical examination was again negative. The laboratory tests in-

Fig. 8. Case IV. Posteroanterior view of the skull showing a large osteoporotic area in the frontal bone.

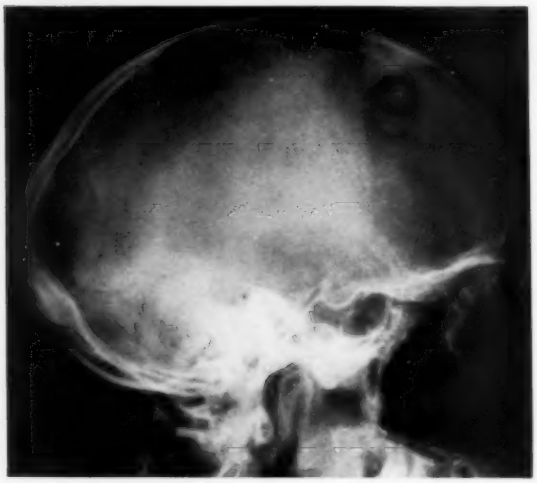

Fig. 9. Case iv. Lateral view of the skull showing the decalcification of the outer table and diploë in the frontal region. Note that the inner table remains intact.

cluding the blood count, blood chemistry, serology, spinal fluid and urinalysis were normal. He was hospitalized for one month and discharged unimproved. The final diagnosis was paroxysmal disorder or epileptic equivalent.

The roentgenograms taken in May, 1931, showed a large, sharply defined area of diminished density which involved the greater part of the left frontal bone and extended across the midline (Figs. 8 and 9). The remaining bones of the skeleton appeared normal. This was, therefore, a case which showed typical osteoporosis circumscripta without any other skeletal changes.

Case v. Hospital No. V.C. 81877. I. W., a Jewish housewife, aged fifty-four, visited the Vanderbilt Clinic on January 1, 1929, complaining of "rheumatism" and stiffness in the right knee of four years' duration and of anterior bowing of the right shin. She also complained of tenderness in the ribs. On physical examination the positive findings were the presence of a "saber shin," with stiffness of the right knee and limitation in mobility of the patella. Moderate hypertension was present. The laboratory examination showed the blood calcium to be between 13 and 16 mg. per hundred c.c.; the blood phosphate averaged about 4 mg. per hundred c.c., and CO_2 about 55 volumes per cent.

The roentgenograms of the entire skeleton showed lesions of typical Paget's disease in the lumbar spine, humeri, pelvis, femora and right tibia (Figs. 10 and 11). Films of the skull revealed a large, sharply defined area of decreased density involving the occipital, parietal and frontal bones (Fig. 12).

Later roentgenograms of the skull taken in August, 1931, showed a number of rounded areas of increased density, in and around the osteoporotic areas, with slight thickening of the outer table and widening of the diploic spaces. Additional films were taken in January, 1932, which showed essentially no change from those taken in August, 1931.

This case had a definite hypercalcemia and showed the gradual transition of osteoporotic lesions in the skull into osteitis deformans within a period of three years.

Case vi. Hospital No. 223356. H. K., a Jewish salesman, aged fifty-nine, came to the Vanderbilt Clinic September 29, 1929, complaining of frequency and nocturia of two years' duration. Three weeks prior to his admission to the clinic his symptoms had progressively grown worse. A benign hypertrophic prostate was removed. Laboratory findings were essentially within normal limits except the blood cal-

Fig. 10. Case v. Lateral view of the tibia showing the typical appearance of Paget's disease.

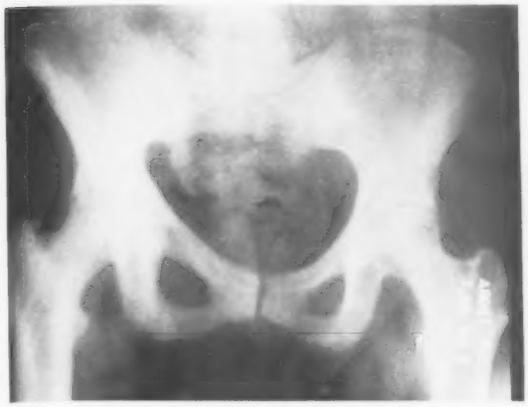

Fig. 11. Case v. Film of the pelvis showing Paget's disease involving all the bones including the upper ends of the femora.

cium which fluctuated from 11 to 13 mg. per hundred c.c.

The roentgen examination of the entire skeleton revealed typical Paget's disease in the pelvis (Fig. 14), lumbar spine, femora, scapulae, and humeri. A large area of osteoporosis circumcripta was noted in the frontal bone. In the parietal region there was a thickening of the outer table and diploë typical of Paget's disease (Fig. 15). In December, 1931, additional skull films were taken, at which time (Fig. 16) new areas of condensing osteitis were seen in and about the region of the osteoporosis in the frontal bone. The roentgenograms of the skull were repeated in January, 1932, and at this

Fig. 12. Case v. Lateral view of the skull showing an osteoporotic area in the frontal bone and a smaller lesion in the outer table and diploë of the parietal bone posteriorly.

Fig. 13. Case v. Lateral view of the skull taken three years after Figure 12, showing the extent to which the disease has progressed. Note the presence of areas of increased density in the frontal bone and a new osteoporotic area involving the outer table of the occipital bone.

time no recognizable changes had occurred since the last examination.

This case demonstrates concomitant lesions of osteoporosis circumscripta and Paget's disease of the skull when the first films were seen. During the two and a half years that the patient was under observation, new areas of increased density appeared in and around the osteoporotic lesions which had increased in size.

Case vii. Hospital No. 185570. G. R. P., a colored dentist, aged thirty-three, was seen in the clinic November 7, 1928, complaining of

Fig. 14. Case vi. Anterposterior view of the pelvis showing advanced Paget's disease.

Fig. 15. Case VI. Lateral view of the skull showing the involvement of the frontal and parietal bones by the osteoporotic process. Note also the osteoplastic lesions.

pain in the lumbar spine and left leg. The trouble began about four years previous to admission with a slight dragging pain in the left groin, radiating into the left thigh. On examination there was definite tenderness over the lumbar segments of the spine. The laboratory findings including serology, blood chemistry and urinalysis were within normal limits. On November 7, 1928, the roentgenograms of the spine and pelvis revealed nothing definitely abnormal. The pyelograms were also reported normal.

Fig. 16. Case VI. Lateral view of the skull taken two and a half years after Figure 15. Attention is called to the increase in the density of the bones in and around the osteoporotic areas.

The roentgenograms of the left leg taken in July, 1931, showed a fusiform expansion of the middle of the shaft of the left tibia. The cortex of the bone appeared thinner than usual along its anterior margin, and a number of coarse trabeculae were present along the middle third of the tibia (Fig. 17). This was thought to be

Fig. 17. Case VII. Lateral view of the tibia to show an early lesion of Paget's disease.

either early Paget's disease or osteitis fibrosa cystica. The skull films showed a sharply circumscribed area of osteoporosis situated in the upper half of the occipital and posterior portions of the parietal bones, mainly involving the outer table and the diploë (Fig. 18). The roentgen examination of the left tibia and skull was repeated six months later and at this time the appearance was practically the same as that of the first examination.

This case illustrates the simultaneous occurrence of osteoporosis circumscripta in the membraneous bones of the skull and early Paget's disease in the tibia.

Case VIII. Hospital No. 273933. M. I., an Italian seamstress, aged forty-four, came to the clinic on October 16, 1930, complaining of burning sensation and pain in the right side of the head. This occurred about two months prior to her admission and was of a half day's duration. At that time she had diplopia which lasted about three weeks. On admission she felt drowsy and tired, and on walking she felt dizzy. The Neurological Department made a tentative diagnosis of encephalitis or brain tumor.

Roentgen examination of the skull revealed an area of osteoporosis circumscripta involving the inner table of the skull and diploë of the right parietal and posterior portion of the frontal bones. In both parieto-frontal regions of the skull there were numerous discrete nodular areas of increased density which were typical of Paget's disease (Fig. 19).

This case showed the combination of osteoporosis circumscripta and osteitis deformans in the skull.

Case IX. Hospital No. 177957. B.B., a Jewish woman, came to the clinic in August, 1928, complaining of urgency, frequency, and dysuria. Cystoscopic examination revealed no evidence of disease. The laboratory tests were also essentially negative. She was readmitted one month later complaining of pain in the right lower back, weakness and occasional night sweats. Physical examination again showed no evidence of organic disease.

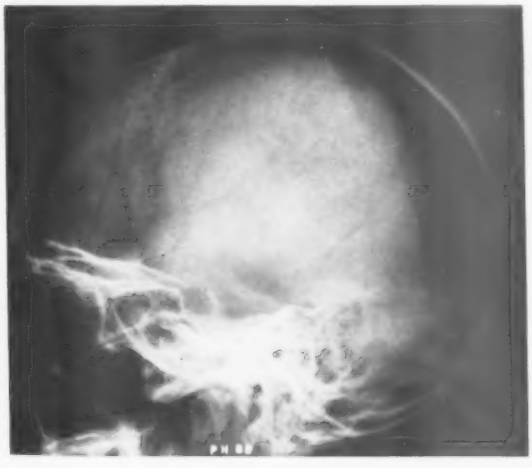

Fig. 18. Case VII. Lateral view of the skull showing the osteolytic area in the parietal and occipital bones.

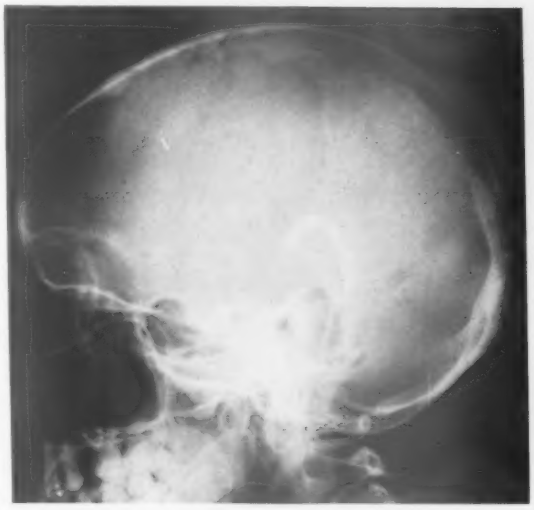

Fig. 19. Case VIII. Lateral view of the skull showing the large decalcified lesion in the fronto-parietal region.

The roentgenograms of the sinuses and skull taken in August, 1928, disclosed a polyp in the left antrum and showed a marked increase in the density of the entire calvarium with widening of the diploic space and thickening of the outer table. In addition, there was a circumscribed area of osteoporosis in the lower half of the occipital bone, and a similar, but not so sharply defined, area of diminished density in the frontal bone, in which were several round dense shadows. Films taken in December, 1931, demonstrated no change in the osteoporotic areas but there was a further increase in the density of the affected parts of the skull.

This case is typical of Paget's disease with osteoporosis circumscripta, in which the condensing phase of the disease predominates.

Case X. Hospital No. 266060. L.L., a Jewish woman, aged forty-eight, was admitted to the clinic August 29, 1930, presenting a large, tender swelling over the anterior portion of the right tibia which had been present one and a half years. The physical examination revealed obesity, and a systolic murmur to the left of the sternum.

The roentgenograms of the right leg disclosed

a marked increase in the density of the right tibia with numerous irregular trabeculae and obliteration of the medullary cavity by new bone production. The skull revealed a large area of decalcification in the frontal and occipital bones. The outer table at the torcular Herophili appeared serrated and thinned. In addition, there were a number of minute, bizarre, calcified deposits along the posterior margin of the osteoporotic area in the frontal bone.

In this case osteoporosis circumscripta was associated with the condensing phase of osteitis deformans in the skull, and moderately advanced Paget's disease in the tibia.

Case xi. Hospital No. 271783. A.T., female, aged sixty-four, was admitted to the clinic October 29, 1930, at which time she complained of pain in the right hip radiating to the sacrum and down the back of the leg. This had been present for seven months. The laboratory examination showed glycosuria.

The roentgenograms disclosed Paget's disease of the spine, pelvis, and femora. The skull appeared diffusely thickened in the region of the outer table and the diploic spaces were filled with numerous shadows of increased density of varying size and shape. These were more abundant in the frontal bone. There were also two large circumscribed areas of diminished density in the frontal and occipital bones.

This case illustrates again the association of Paget's disease of the skull and other bones with osteoporosis circumscripta in the calvarium.

Case xii. Hospital No. 318174. L.T., a colored woman, aged twenty-seven, was admitted to the clinic October 7, 1931, complaining of swelling in the right inguinal region of thirteen years' duration which was diagnosed as granuloma. On November 2, she returned to the clinic complaining of severe headaches. On examination there was slight anterior bowing of both tibiae. The blood Wassermann was 4 plus.

The skull films revealed an area of osteoporosis in the frontal bone in which there were a few rounded shadows of increased density. The outer table and the diploë appeared thinner than usual. Both tibiae showed changes of osteitis deformans.

This was the only case in the series in which syphilis was associated with Paget's disease.

Discussion

The fact that only 10 cases have previously been recorded in the literature would lead one to believe that osteoporosis circumscripta is rare. In this paper we are reporting 12 additional cases encountered in routine roentgenographic examinations during the past three years, which would indicate that the disease is not uncommon.

The symptoms presented by these patients varied. Three (Cases ii, iii and viii) had pain referable to the head. There was no external evidence of the disease in any case. Only one had a positive Wassermann reaction (Case xii). Blood calcium studies were made in 3 cases; in only one was there a definite hypercalcemia (Case v).

By comparing the characteristic features of Paget's disease and osteoporosis circumscripta in the skull their close relationship may be more clearly appreciated. A review of our cases shows the age period of osteoporosis circumscripta to be the same as that of Paget's disease. Our youngest patient was twenty-seven while the oldest was seventy years of age. Eight of the 12 patients were women and 4 were men.

Typical Paget's disease of the skull consists of various degrees of thickening of the tables with numerous deposits of increased density, interspersed with irregular, mottled areas of diminished density. In osteoporosis circumscripta there is a sharply delineated area of diminished density which frequently contains, within and around it, areas of increased density (Cases i, v, vi, ix, x, xi and xii). Furthermore, in many cases of Paget's disease of the skull the entire background is osteolytic, and upon this structure are placed the denser shadows of varying size and shape. Either lesion may be localized in any part of the skull but usually more than one bone is involved. It is interesting to note that in some of our cases the outer table was involved while the

inner table and diploë appeared to be intact, and in others only the diploë and outer table were affected. This has led us to believe that the earliest manifestations of the disease are to be found in the external table of the bones of the skull. In Paget's disease the outer table and diploë are likewise first involved and even in advanced cases the inner table is often relatively intact (Fig. 1). Moreover, in osteoporosis circumscripta the bone may be thickened as in Paget's disease.

There seems to be an apparent affinity for the membranous bones of the skull, but in some cases the cartilaginous bones are also extensively involved. The apparently more frequent and extensive involvement of the membranous bones may be due to the fact that the lesion is more readily recognized in the bones of the vault and also that minor changes of the bones of the base of the skull are more difficult to interpret in the roentgenogram. When the disease affects the bones of the base they do not become osteolytic but instead they become denser than normal as in Paget's disease, and there is a marked exaggeration of the trabeculae (Fig. 3).

Up to the present time, in our entire series, the bones of the skull have been the only ones involved by osteoporosis circumscripta. In fact, the only point of dissimilarity between the two diseases is the absence of the osteoporotic lesions in other parts of the skeletal system.

Three cases (V, VI and XI) showed well-advanced, multiple lesions of Paget's disease in the osseous system (Figs. 11, 12 and 14), while another group of 3 (Cases VII, X and XII) had a lesion in the tibia only. Two of the remaining 6 cases showed no other bone involvement than that of the skull. The rest of the skeleton of the remaining 4 cases was not studied roentgenographically.

Five cases were followed for periods of from six months to eight years (Case 1, 8 yr.; IX, $3\frac{1}{2}$ yr.; V, 3 yr.; VI, $2\frac{1}{2}$ yr.; VII, 6 mo.). In Case 1, followed for eight years, the evolution of the disease is well demonstrated in the films (Figs. 2 and 3). The development of the typical mottled appearance of Paget's disease in and about areas previously showing osteoporosis circumscripta is well shown in the films. The follow-up period in the other patients was too short to show any remarkable change in the disease. From the cases at hand it appears that a year or more must elapse between roentgen studies before any recognizable change in the condition will be apparent.

The changes found in the skull of the patient reported by Whitlock are quite similar to those in our Case 1. The lateral view of the skull shown in his article discloses a very extensive circumscribed area of diminished density occupying practically the anterior two-thirds of the calvarium, interspersed with numerous areas of increased density, particularly in the frontal region. He described this as a direct extension of an adamantinoma. We believe, however, that the adamantinoma of the upper jaw might well have been coincident with Paget's disease and osteoporosis circumscripta in the skull rather than being directly related to it. We have found osteoporotic changes in the bones of the skull far removed from the region of the jaw. If these areas were due to metastases from the adamantinoma one would have to presuppose that they took place through the lymph or blood stream. This would be very unusual, for this type of tumor ordinarily grows by direct extension. Furthermore, adamantinomas frequently occur as bucconeural pouch tumors. Many of these have been reported in the literature and we have seen a number of them. We have never observed a patient with a bucconeural pouch tumor in whom there were also osteoporotic changes of this kind in the skull, nor are we aware of such a case in the literature. Examination of the oral cavity and the roentgenograms of the facial bones of our patients failed to reveal any evidence which would suggest an adamantinoma. For these reasons it seems probable that the changes in the skull de-

scribed by Whitlock were entirely independent of the adamantinoma of the superior maxilla.

The evidence from this series of cases indicates that osteoporosis circumscripta is the osteolytic stage of osteitis deformans rather than an independent and rare manifestation of it, as suggested by Weiss. It is true that he has followed one of his cases for about three years and in that time no bony changes suggestive of Paget's disease have appeared. The only explanation we can offer is that in his patient the condensing phase of the disease is apparently in abeyance. In one of our cases, films of the skull taken eight years after the first examination showed the complete picture of osteoporosis circumscripta combined with osteitis deformans.

From this evidence it would appear that osteoporosis circumscripta is a form of, or precursor to, Paget's disease where the osteolytic or the rarefying phase predominates. It appears to us that the term osteoporosis circumscripta should no longer be used to denote a disease entity but rather to modify the term Paget's disease.

DIFFERENTIAL DIAGNOSIS

Osteoporosis circumscripta must be differentiated from multiple myeloma, metastatic carcinoma, xanthomatosis and endothelial myeloma. In multiple myeloma there are usually numerous worm-eaten, punched out areas, while osteoporosis circumscripta usually appears as a single large focus of halisteresis. Furthermore, in multiple myeloma there is no bone production anywhere in the osseous system. It is a purely destructive process. In osteoporosis circumscripta examination of the rest of the skeleton may reveal lesions characteristic of Paget's disease. The characteristic feature of osteoporosis circumscripta is not only that of decalcification but also of definite alteration in the structure of the bone. Indubitable destruction of the bone as seen in multiple myeloma does not occur in osteoporosis circumscripta. In the rare case in which roentgenographic differentiation cannot be made, the laboratory examination and history may aid in establishing the correct diagnosis. These differential points also hold true in osteolytic metastatic carcinoma. Xanthomatosis is usually found in children and is characterized by the involvement of the skull and other flat bones with frequent association of diabetes insipidus, gingivitis and exophthalmos. The lesions are usually multiple and show remarkable improvement with radiation therapy. Endothelial myeloma or Ewing's tumor must also be differentiated from osteoporosis circumscripta. Ewing's tumor practically always occurs in patients under twenty years of age. The course of the disease is more rapid and, in addition, a leucocytosis and slight fever are generally present in a majority of the cases.

SUMMARY AND CONCLUSION

1. Twelve cases of osteoporosis circumscripta of the skull are presented, 6 of which showed the characteristic picture of Paget's disease elsewhere in the body. Osteoporosis circumscripta in 8 cases was associated with Paget's disease in the skull. Five cases were under observation for eight, three and one-half, three, three and one-half years and six months, respectively; in 4 of them there was a definite progression of the lesion with typical Paget's disease developing in and around the osteoporotic areas.

2. Osteoporosis circumscripta may precede typical Paget's disease of the skull.

3. Osteoporosis circumscripta is frequently associated with typical Paget's disease in other bones.

4. Osteoporosis circumscripta, like Paget's disease, usually attacks the outer table of the skull first.

5. From a study of these twelve cases, it appears quite certain that osteoporosis circumscripta and osteitis deformans are one and the same disease.

We wish to thank Dr. Frederick H. Baetjer for the privilege of using the film reproduced in Figure 2.

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THE ADVANTAGES OF ROENTGENOSCOPIC CONTROL IN ROENTGENOGRAPHY OF THE STOMACH*

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THE earliest roentgenologic work on the gastrointestinal tract was naturally done with the roentgenoscope since apparatus was not available to make rapid exposures. As the exposures required several seconds, the movement of the organs blurred the image and the defects caused by organic lesions were not visible. Because of this fact, diagnostic signs were developed which were best discovered by the roentgenoscope. As an example I mention hyperperistalsis, skipping of a diseased area by peristaltic waves, tenderness to pressure over a suspected area, fixation, etc.

When apparatus had improved to a point where exposures of the abdomen could be made in a fraction of a second, Cole revolutionized gastrointestinal diagnosis by his monumental work demonstrating that the diagnosis of an organic lesion in the stomach or duodenum depended upon the actual visualization of that lesion on the roentgen plate. Before that time diagnosis had largely been made inferentially by a combination of signs and symptoms generally referred to as a "symptom-complex." Cole's work was so conclusive that it could not be ignored, but it was only natural that many members of the profession were loath to discard entirely a method that had been in use for several years and which experience had taught them had considerable practical value.

As a consequence a controversy waged for several years over the respective values of the roentgenoscopic and the plate method of diagnosis. This argument helped to emphasize the merits of both methods and as a result, when the conflict died away, most American roentgenologists were convinced that both had value. Today, probably a very large majority of our profession in America use both the roentgenoscope and the roentgen film in gastrointestinal diagnosis.

However, the older members of the profession seem to have forgotten and probably the younger members never knew that Cole's early work was done on a "Cole table." On this apparatus each exposure was watched in a reflecting roentgenoscope and in this way the exposures could be so controlled as to demonstrate what was seen in the roentgenoscope. The "Cole table" does not seem to be in very general use today, but I believe it is still true that diagnosis will be more accurate if the exposure of the film is controlled by roentgenoscopic observation. By this I mean that the exposure should be made in such position and under such conditions as previous roentgenoscopy has shown proper to demonstrate the lesion. To accomplish this it is usually necessary that the patient shall not be moved from the roentgenoscopic apparatus to have the roentgenograms made.

If pressure must be made to visualize the lesion this fact is, of course, obvious. However, it seems to be rather common practice in some clinics to roentgenoscope patients in one room and send them into another to have the roentgenograms made. From many years' experience in roentgenoscopy I am convinced that the slightest change in the position of the patient may at times obliterate the deformity caused by an organic lesion. In such a case, unless the patient is placed in exactly the proper position, any number of exposures will fail to visualize the lesion. To attempt to put the patient in that position after removing him from the roentgenoscope to another piece of apparatus is a very uncertain procedure and will succeed only by good luck and not by good judgment.

In general, European roentgenologists

* Read at the Thirty-second Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 22–25, 1931.

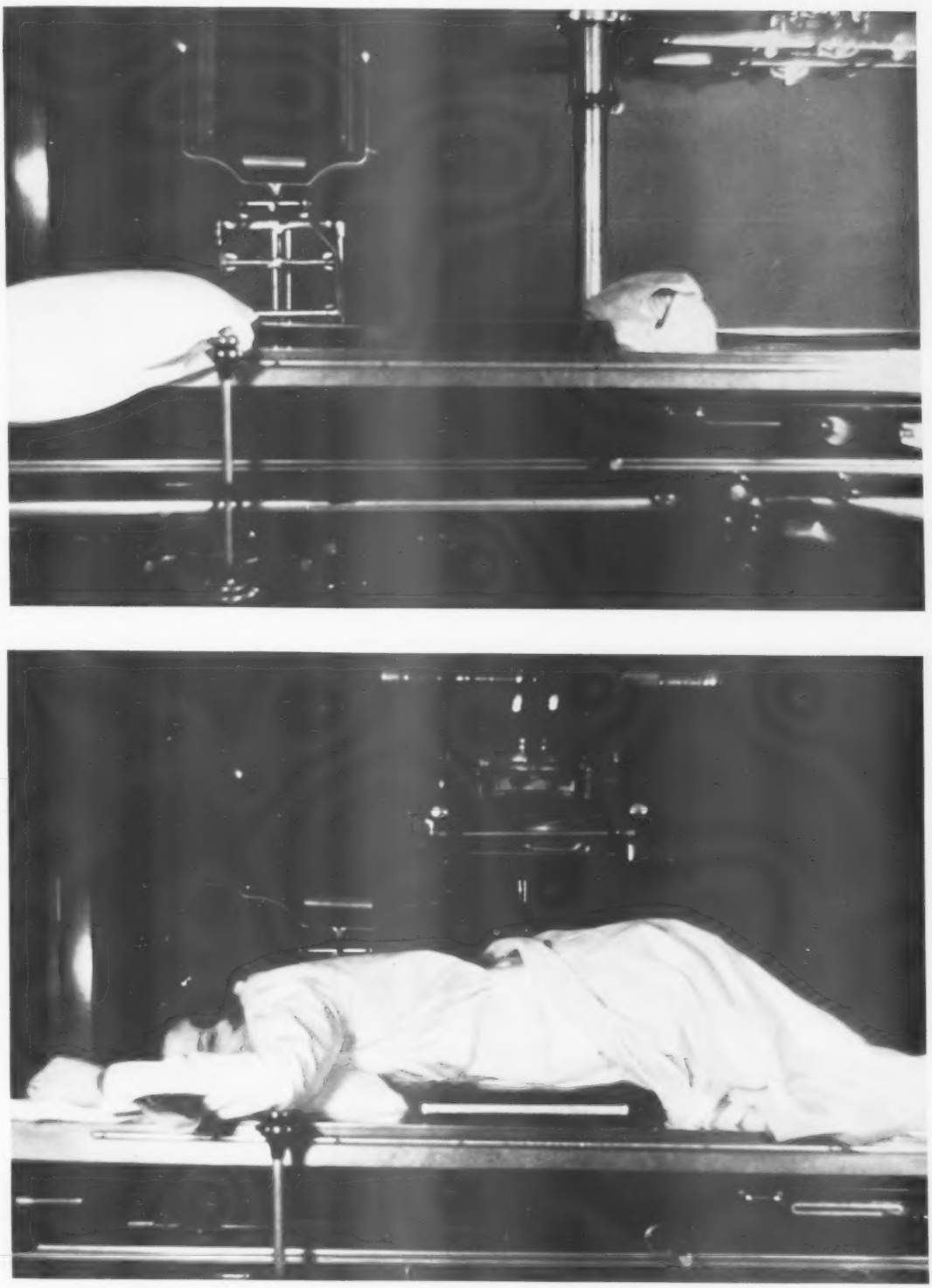


Fig. 1. The simplest form of tunnel for exposures in the prone position.

seem to appreciate this and their technique has always been to make the film exposures on the roentgenoscopic apparatus. I believe this method is not only more accurate, but is also more economical of time, although the latter view does not seem to be generally accepted.

At first thought it might seem easier after the roentgenoscopy is finished to send the patient into another room to have the films made while the roentgenoscopist goes on with the next case. However, the patient is often too ill to move quickly, his surroundings are unfamiliar and he has to be guided to the place where he should go; while the roentgenoscopist is presumably well and knows just what to do and where to go. He should be able to make the necessary transfer in half the time it requires to move the patient.

If adjoining rooms are fitted up to do both roentgenoscopy and roentgenography in each, he can step from one to the other, roentgenoscoping patients in either room while the films are being made in the other. By this method the patient can be kept in exactly the proper position on the roentgenoscope until the films are made.

It does not require any additional rooms to work in this manner, but of course extra roentgenoscopic apparatus is necessary and each roentgenoscopic table must have a tube stand beside it. When this apparatus is not being used for roentgenoscopy it can, of course, be used for general roentgenography, Bucky or otherwise, as desired. It costs slightly more to equip in this manner, but the greater accuracy and elimination of unnecessary exposures justify the additional expense. Where the amount of work is small it can be done expeditiously in one room with much less effort and with less apparatus. I have used this system now for about fifteen years and am convinced that it is more accurate and more economical than the practice of roentgenoscopy in one room and roentgenography in another.

For exposures in the upright position nothing extra is needed, the film being placed behind the roentgenoscopic screen and the exposure made with the roentgenoscopic tube.

The exception to this is the pressure method of visualizing lesions which has been advocated by various European workers, notably Berg, Åkerlund and others. The devices which they use have been described in the literature. I have not had enough experience with this method to discuss it with authority, but if the claims made for it are accepted, it is a very strong recommendation for my argument that exposures should be made by roentgenoscopic control. With the exception of lesions which are demonstrated by pressure or manipulation, it has been my experience that a much larger percentage are discovered in the prone than in the erect posture.

It is not satisfactory to make the exposures in the prone position with the roentgenoscopic tube, since the patient must lie face down in order to get proper filling of the stomach and if the film is placed on the patient's back, the distance from stomach to film is so great that the image is too blurred to be reliable. I worked in this way for some time several years ago, but the method was unsatisfactory.

If the lesion shows best with the patient lying on his back it is then, of course, quite simple to lay the cassette on his abdomen and make the exposure with the roentgenoscopic tube. However, the great majority of lesions are either in the pyloric end of the stomach, or in the duodenum, and these are usually best demonstrated with the patient lying face down.

There are very few cases in which a satisfactory image is obtained with the patient lying flat on the abdomen. Usually this causes pressure against the body of the stomach and produces an artefact which, even if recognized for what it is, obscures that portion of the stomach and makes recognition of a lesion in that location impossible.

Also, with the patient lying flat, emptying of the stomach is often poor so that the duodenum does not fill well. By a slight

rotation of the patient the stomach empties freely and the pylorus and duodenum can be seen satisfactorily.

In a general way, the stomach of a fat individual empties better when he is turned toward the right side, and that of a thin person empties better if he is turned a little toward the left side. Usually a pillow or sand bag under the pelvis improves matters by relieving the pressure caused by the patient's weight against the anterior abdominal wall.

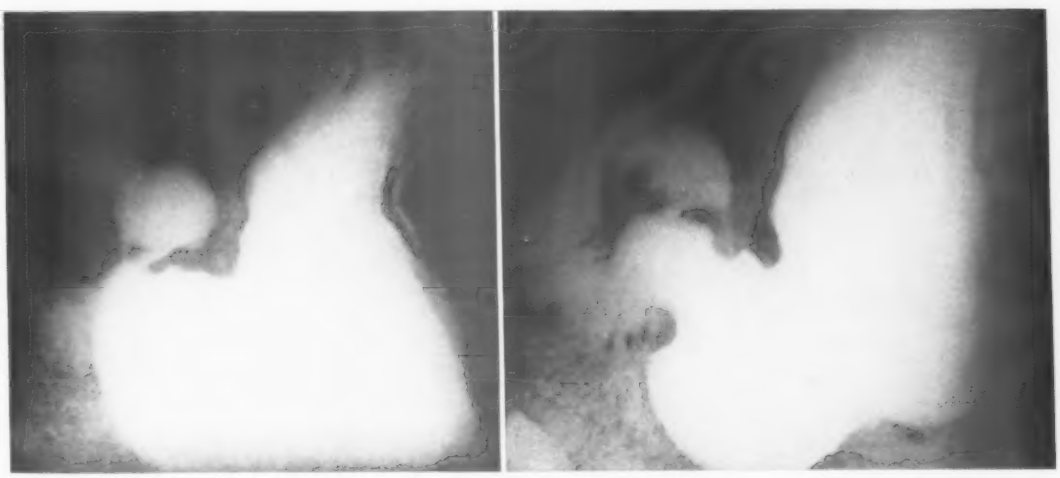
Some patients show an undistorted stomach shadow only at the end of a full inspiration; others do better by simply suspending respiration; still others after both full inspiration and full expiration.

These factors are all matters of experiment in each case and must be tried in order to demonstrate either a deformity or a normal contour, as the case may be. Having determined which is best, the exposures are made in exactly the same way.

Having reached this point, a simple way to proceed is to slip a plate tunnel under the patient, readjust him under the roentgenoscope to the proper position and make as many films as desired by means of a tube above the patient's back.

If exposures with the Potter-Bucky dia-

Fig. 2. Pressure deformity on greater curvature relieved by rotation of the patient.



a *b*

Fig. 3. (*a*) Annular carcinoma at the pylorus. (*b*) Not seen after the patient is rotated.

phragm are desired, the process is still more simple as the Potter-Bucky diaphragm can be moved into position without disturbing the patient at all. All makes of roentgenoscopic tables are obtainable with Potter-Bucky diaphragm attached. I prefer not to use the Potter-Bucky for this purpose.

If the chosen technique requires numerous exposures on one film, this can be accomplished either with a simple tunnel slipped under the patient after roentgenoscopy is finished, or by the use of more elaborate apparatus which may or may not be a part of the table. The apparatus used by Potter is ideal for this purpose. It does not interfere with roentgenoscopy and greatly facilitates the making of the exposures. It is easily removed from the table after the work is finished so that the table can be used for other purposes.

If the technique adopted necessitates moving the patient in order to introduce the plate-holding device, this device must be transparent to the roentgen ray so that roentgenoscopy can be carried on through it after it is placed in position in order to make the necessary observations. It may be argued that if the pathology or absence of it is determined by the roentgenoscopic examination, why go to so much trouble to show it on the films. This argument would be valid if no films were made at all. The roentgenoscopist's word as to what he saw would then be final. However, if films are made and they do not show what the roentgenoscopist believes he saw on the screen, there may be some difficulty in convincing the referring physician that the roentgenologist's memory is more accurate than the films which he sees before him. Aside from this it is only natural for the roentgenologist himself to attach more weight to the evidence seen on the film as time elapses after the examination and his recollection of the roentgenoscopic image becomes more uncertain. If the roentgenoscopic notes and the roentgen films do not agree, the average roentgenologist is almost certain to make his final diagnosis from the film.

It is true that the film will often show pathology which was not seen on the roentgenoscopic screen. In such a case naturally one is not using the film to record something seen in the roentgenoscope. However, even in these cases the roentgenoscope helps by determining the proper position to avoid pressure defects and to assure free emptying and a filled duodenum. Occasionally one sees an area in the roentgenoscope which does not look exactly normal and the better detail of the film shows the presence of a lesion in that location. Probably the greatest use of roentgenoscopic control is the avoidance of pressure defects, as above suggested, and also the placing of the patient in such a position that the stomach empties freely.

If the barium meal leaves the stomach so slowly that it runs out of the duodenum as fast as it runs in, the duodenum will never be fully distended and this partial filling may be mistaken for an organic deformity. Changes in the patient's position often alter the emptying rate considerably. It is just as important to recognize that the stomach and duodenum are normal as it is to demonstrate disease; and the roentgenoscope often permits this by enabling one to avoid the artefacts referred to.

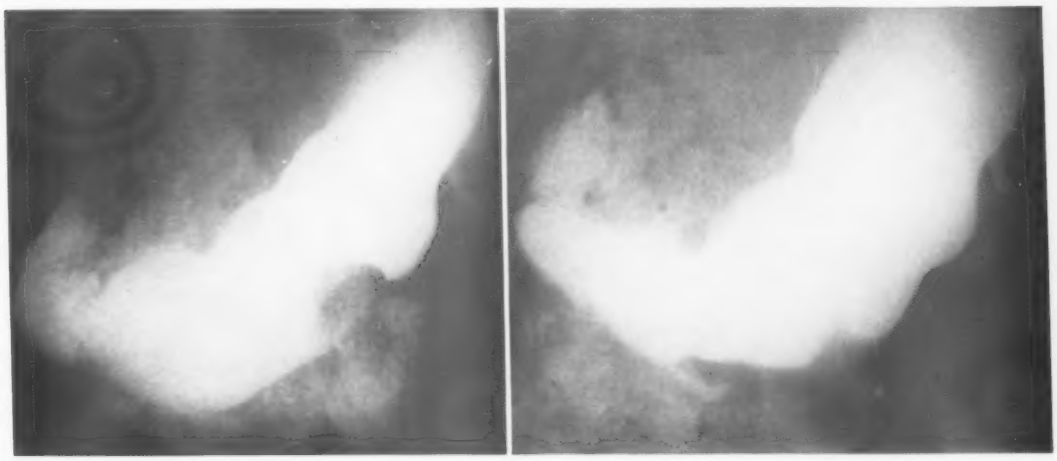
It is obvious that filling defects caused by changes in the stomach wall will show best when seen in profile, and changes in the position of the patient may be necessary to bring this about. Fortunately for roentgen diagnosis, organic lesions are usually accompanied by considerable muscular spasm and the ensuing deformity is almost always larger than the actual lesion. For this reason they can generally be detected through quite a considerable range in rotation of the patient. However, cases are seen occasionally in which the least change in position obscures the lesion.

Within the last six months I have seen two cases of carcinoma, one of the annular type at the pylorus and the other a large medullary growth of the greater curvature, and in both of these a slight change in the position of the patient totally obscured all

evidence of their existence. The medullary lesion was as large as half a lemon. To have missed this lesion would have been a very serious roentgenological error. It was seen on the roentgenoscope, but the first set of films made did not show it, evidently because the patient had moved after being placed properly as she was not very tractable. A second set of films made more carefully demonstrated a very large tumor of the body of the stomach.

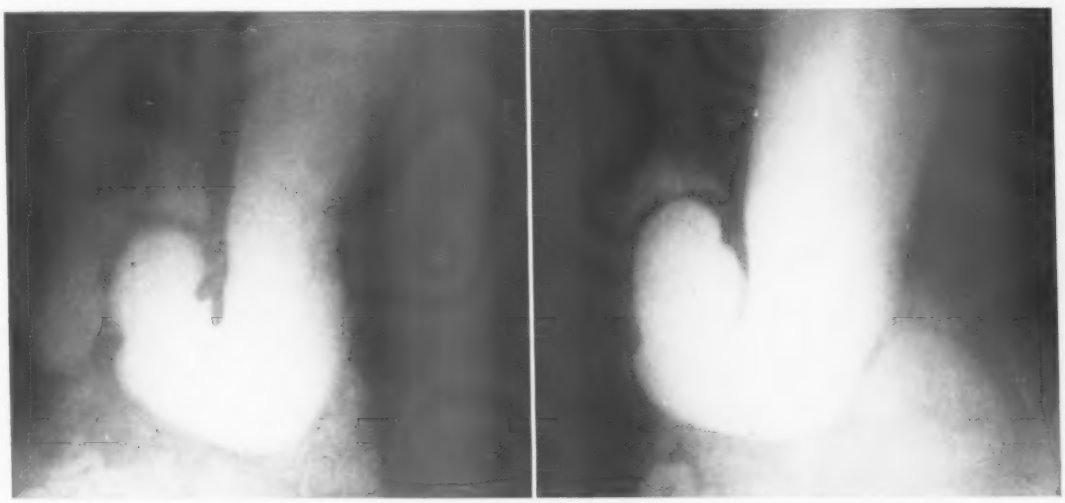
The case of annular carcinoma at the pylorus was also recognized by roentgenoscopy and films were made to demonstrate it. The patient was then deliberately rotated first to the right and then to the left, and in both these positions the typical deformity disappeared. Films were made in these positions to demonstrate the truth of what I am attempting to prove in this article.

The niche of a gastric ulcer often disappears when the patient's position is changed and I also believe it is possible to obscure the deformity of a duodenal ulcer, although not so easily.



a *b*

Fig. 4. (*a*) Large carcinoma of the greater curvature. (*b*) Deformity disappears when the patient is rotated.



a *b*

Fig. 5. (*a*) Dilated second portion of duodenum from obstruction due to carcinoma, apparently primary in the pancreas. (*b*) Dilatation not shown.

I had thought for years that the demonstration of an unbroken outline in the first portion of the duodenum was proof that duoenal ulcer did not exist. I have recently seen a case of proved duodenal ulcer which was easily demonstrated by the roentgen ray, but when the patient was turned to a certain position the outline of the "cap" was perfect. If the only evidence available had been a number of films made in this particular position, the ulcer would certainly have been overlooked.

Duodenal diverticula are easily obscured by changes in position. I surmise that a more correct statement would be that they are quite difficult to visualize except in exactly the right position.

Partial obstruction in the lower duodenum is likewise only demonstrated in certain positions. Often this shows best with the patient lying on the back or slightly rotated to one side or the other. The least change in position will often throw the shadow of the descending duodenum behind the stomach and the lesion will not be recognized.

It hardly seems necessary to cite further specific instances to convince the reader that organic lesions of the stomach or duodenum may be recognized with the patient in certain positions and under certain conditions and not others. A little observation on the part of anyone will soon convince him of this fact.

The purpose of this article is rather to call attention to the fact that the exposures in gastrointestinal cases should be made on the roentgenoscopic apparatus, and that it is actually easier and quicker to do it this way than to move the patient elsewhere. The greater accuracy obtained and the smaller number of re-examinations necessary are in themselves sufficient justification for this method.*

* For discussion see page 222.

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EVALUATION OF COMPRESSION TECHNIQUE IN THE ROENTGEN DEMONSTRATION OF DUODENAL LESIONS*

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DURING the past ten years numerous contributions have appeared, chiefly in European journals, describing the advantages of procuring roentgenographic studies of the gastrointestinal mucosa. While their methods of obtaining mucosal patterns in relief have slight technical variations, their purpose and result are the same, namely, the roentgenographic demonstration of localized portions of the gastrointestinal tract.

The purpose of this study is an attempt to evaluate the method as it applies only to the study of the duodenum and more particularly the cap.

Two methods of obtaining local compression were used in this study: the Chaoul compressor and the rotating spiral diaphragm designed by Åkerlund. The Chaoul compressor consists of a small rubber bladder surrounded by a hard rubber ring 6 inches in diameter. This is encased in a canvas belt which is strapped around the patient. The bladder may be inflated to any desired degree by a simple hand bulb having a two-way valve. The ring is centered over the duodenal cap and the bladder inflated to a moderate degree. Instead of strapping the belt tightly and depending entirely on inflation of the rubber bladder for compression, we have found it most advantageous for the patient to hold each thumb and index finger about the periphery of the ring while a cassette is applied directly against the bag with varying degrees of pressure during succeeding exposures. Roentgenographic studies in which compression is used are all made during the course of the roentgenoscopic examination and, except in rare cases, in the erect position. It is essential to make a number of films with the cap under various degrees of compression as even with short exposure time a few films will show motion. Moreover, it will be found that an ulcer niche is often visible only on films made under a certain degree of compression. Lesions of the anterior wall, particularly, are shown to best advantage under light compression. It is essential to use slight and marked obliques for localization of a visualized lesion. As a rule, the best roentgenograms are obtained with the patient turned just enough to throw the cap away from the spine. Exposure time is necessarily short. It is rarely necessary to use more than 0.5 second and most exposures are made between 0.2 and 0.4 second.

It is desirable to obtain some views of the cap after the patient has swallowed an ounce of fairly thin, watery barium mixture. To obtain compression under roentgenoscopic observations I have found the ordinary large aluminum kitchen spoon most satisfactory. After a roentgenoscopic study of the esophagus, stomach and cap, the compression device is centered over the area desired and films made in the different positions under varying degrees of compression. Further films are made after the routine barium meal and roentgenoscopic study. The above method has been used routinely as a supplementary procedure in all gastrointestinal tract examinations during the past eighteen months.

The early indirect criteria for the diagnosis of duodenal ulcer were obviously inadequate, and between 1910 and 1920 the literature contains numerous contributions regarding direct signs of ulcerating lesions. Among these the observations of Cole, Case, Haudek, Carman and Åkerlund[1]

* Read at the Thirty-second Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 22–25, 1931.

Fig. 1. Normal cap under compression.

are outstanding. Following the early communications of Cole, Chaoul[14] described a method in which he used a compression tube to apply local pressure to the duodenum and during the application of this pressure made roentgenograms of the part under examination. Later, Åkerlund's contributions stressed the demonstration of niche evidence, his earlier reports showing a 60 per cent niche incidence.[1] In later contributions his descriptions of niche types and their methods of demonstration are classical.[2] He found that "the roentgenological niche symptom in duodenal ulcer is neither a rare phenomenon nor difficult of interpretation. The bulb niche may have for its anatomical basis all possible stages of ulcer formation, from penetrating or callous ulcer to superficial nonindurated ulcer. Even fossa shaped depressions may manifest themselves as roentgenological niches." In a later report he says "the anatomical basis for the roentgenologic bulbus niche is rarely a penetrating ulcer but usually an induration of the duodenal wall surrounding the ulcer. The

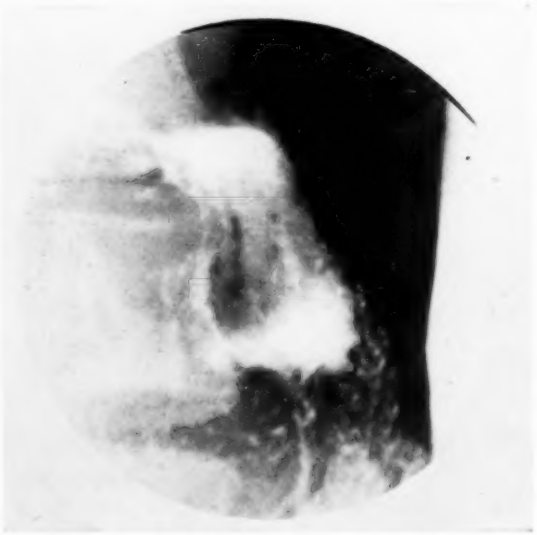

Fig. 2. Normal cap under compression.

Fig. 3. Normal cap under compression.

dimensions of the bulbus niche vary from the size of a pinpoint to that of a walnut. Occasionally there may be present a villus-like projection at one side of the niche. Occasionally the niche shadow is extremely dense and at times it is poorly demarcated; occasionally a small gas vesicle may be seen under the cupola of the niche. The bulbus niche has a definite point of predilection for the lesser curvature. The bulbus niche is frequently accompanied by other deformities which facilitate the diagnosis."

Particularly pertinent is another statement of Åkerlund's. "In a number of cases

which were periodically examined by us we could watch the disappearance of the ulcer niche, while the bulbus defect remained." In 1927 Akerlund[2] cited further experiences with compression technique, finding that he was able to demonstrate multiple bulbar niches with increasing frequency, showing three and even four niches in some cases.

Other reports on the use of compression technique also show a high percentage of niche demonstration. Berg[9,10] finds niche evidence in a little more than 50 per cent of his cases. Albrecht's[6] percentages seem unreasonably high. He reports niches in

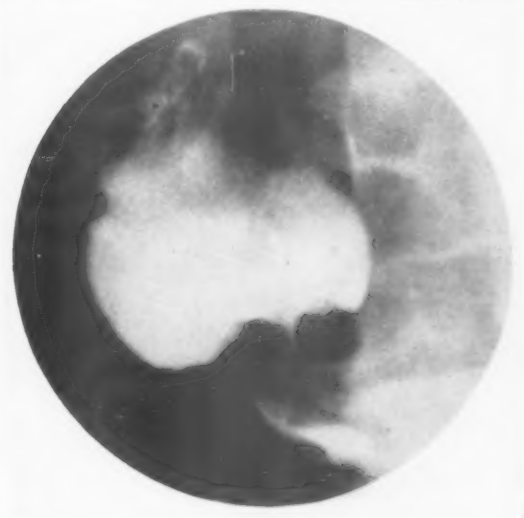

Fig. 4. Barium-filled cap. No characteristic ulcer deformity.

90 per cent of a series of duodenal ulcers and found two niches in one-third of his cases. Diamond reports two-thirds niche evidence in a small group of duodenal ulcers while Carman and Sutherland[13] report niche demonstration in 13.27 per cent. Boman,[12] first American to report his experiences with compression technique, found it a means of obtaining direct evidence of ulcer in a larger number of cases but gave no niche incidence. Kirklin[20] reports 15.24 per cent niche evidence in the form of flecking in 1,791 duodenal ulcers seen at the Mayo Clinic in 1930. Akerlund,[4] in recent communications, reports 75 per cent niche visualizations.

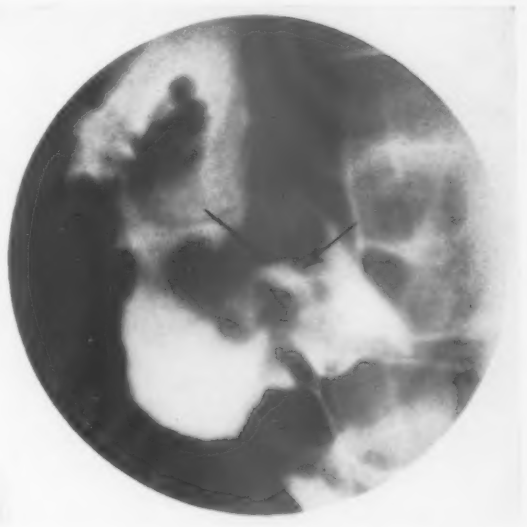

Fig. 5. Same cap under compression showing niche in relief.

That roentgenoscopy alone is not conclusive for the demonstration of niche is indicated by the fact that only 22 per cent niche incidence was noted on one of our services where the roentgenoscopic-roentgenographic switch-over facilities were inadequate for compression technique during a large part of 1930. In the same year we showed niche in 41 per cent of bulbs having

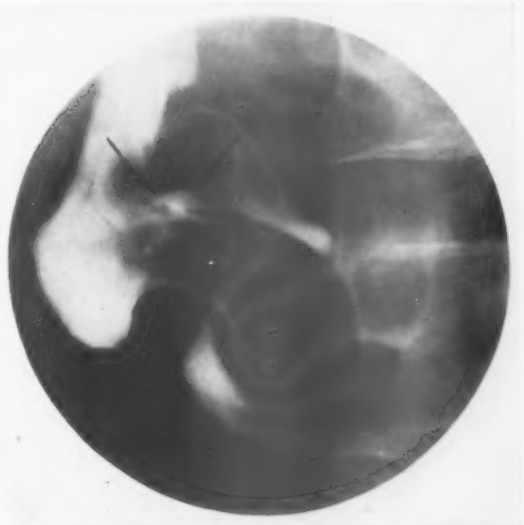

Fig. 6. Another view of cap shown in Figure 4. Note change in niche contours with different degrees of compression.

Fig. 7. Marked bulbar deformity without compression.

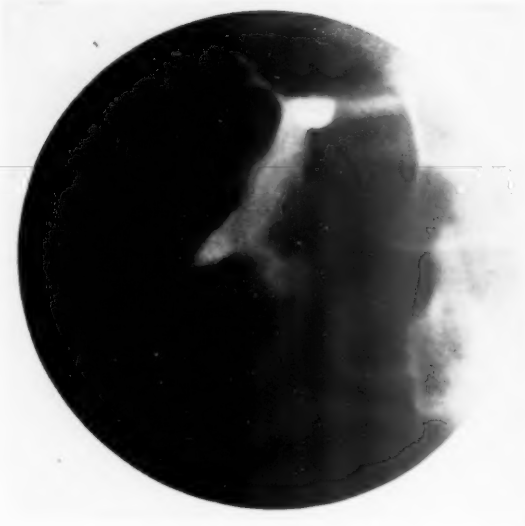

Fig. 8. Same cap under compression showing niche.

a deformity characteristic of duodenal ulcer. In the past six months, due to improved accuracy of technique and interpretation, we have shown niches in 64 per cent.

The individual reports of various roentgenologists on niche incidence are not quite comparable, mainly for two reasons: (1) There is insufficient unanimity of opinion as to what constitutes niche evidence. (2) Not all roentgenologists are employing a technique in which compression is used in obtaining some views of the duodenal cap. While roentgenograms of barium-filled duodenal bulbs will show unmistakable niche evidence in a small percentage of cases, the majority of niches are not clearly visualized unless compression is used. It would seem that more uniform technique and a more universal conception of what constitutes a niche, as based on the observations of Cole,

Fig. 9. Apparently normal cap without compression.

Fig. 10. Same cap under compression showing two ulcer niches.

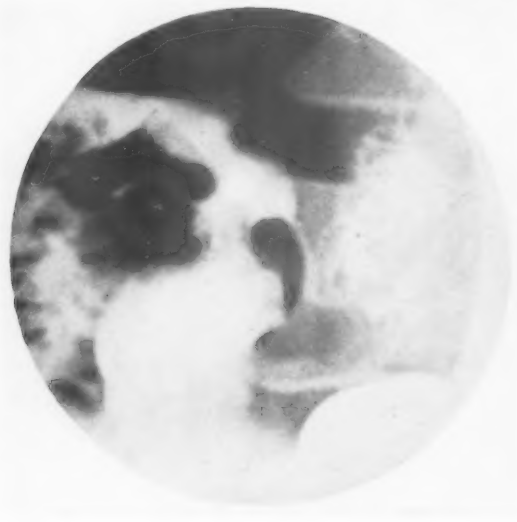

Fig. 11. Characteristic ulcer deformity.

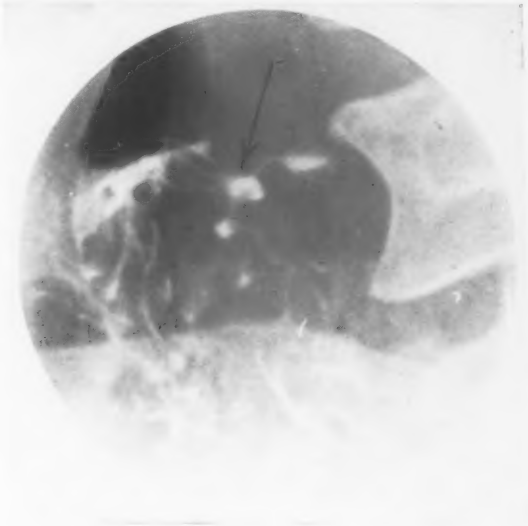

Fig. 12. Same case with compression showing central niche.

Haudek, Berg and Åkerlund, would tend to correct the discrepancy of niche findings.

True niche visualization is of course important evidence of ulcer and regarded by some roentgenologists as the only irrefutable roentgen sign. We do not feel that other roentgen evidence of ulcer should be minimized because one happens to be using compression technique in the course of the roentgen examination. With compression technique, the percentage of niche findings is markedly increased. While evidence of niche is occasionally seen on films made without compression, the niche does not stand out with any great degree of detail. In many ulcers of the variety described by Cole in his early writings, the cap may be sharply contracted about the lesion and compression here is of no particular advantage. However, in views of

Fig. 13. Abnormal cap without compression.

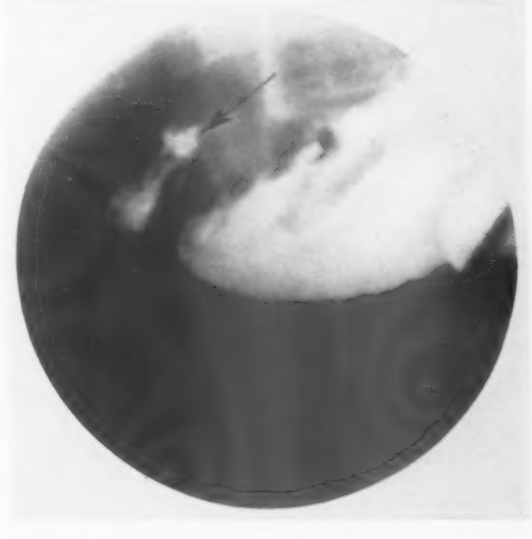

Fig. 14. Same cap under compression. An ulcer niche is now clearly visible.

Fig. 15. Compression reveals irregular niche with stellate arrangement of mucosal folds.

Fig. 16. Same cap after eight weeks of medical treatment. Niche has disappeared. The patient is now entirely free of symptoms.

most barium-filled caps it is impossible to draw very accurate conclusions as to the size and site of a lesion unless mild local compression is used to accentuate the localized pathology. This is well shown in Figures 21 and 22.

It is surprising how frequently niche evidence of one and occasionally two duodenal ulcers can be demonstrated in a series of roentgenograms made with the cap under various degrees of compression (see Figs. 4, 5, 6, 21 and 22). One must be careful, however, not to be too enthusiastic in looking for multiple niches, as frequently a pocket-like retention will be very misleading.

Most cases of duodenal ulcer show evidence of contour deformity in some positions, but occasionally a superficial en face

Fig. 17. Filled cap shows deformity but no visible niche.

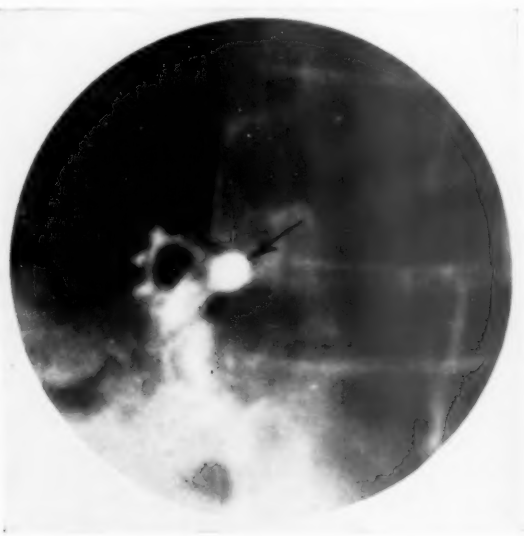

Fig. 18. Same case with compression. The niche is now clearly seen.

FIG. 19. Barium-filled cap.

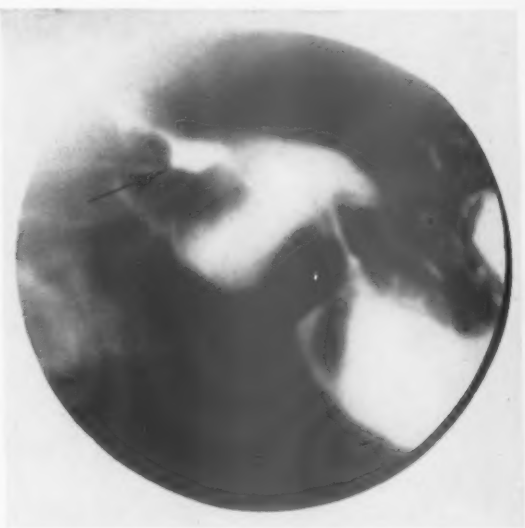

FIG. 20. With compression a rather large niche is visualized at the apex of the cap.

ulcer may present no demonstrable contour defect (Figs. 26 and 27). In this type, compression technique is of particular advantage as with its use even the flat niche will stand out sharply and with great detail. In views of such a cap well filled with barium the niche may show as a spot of slightly greater density, but the difference is very slight and this finding will frequently escape recognition unless one has already examined films of this cap under compression.

Evidence of niche is particularly valuable as a means of showing response to medical treatment. When patients on whom a diagnosis of duodenal ulcer has been made return for re-examination, roentgenograms of the barium-filled deformed cap often cannot be differentiated from those made before treatment. The character of de-

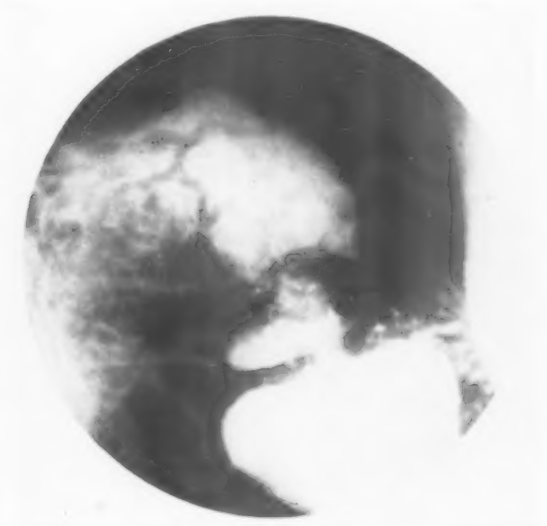

FIG. 21. Deformed cap without compression. Niche is seen but poorly defined.

FIG. 22. Same cap under compression. Well-defined niche is now seen.

Fig. 23. Rather large niche near base of cap. This appearance is frequently simulated by barium retention in superior recess when bulb is compressed.

formity is frequently identical. Roentgenoscopically there may be a change in the picture; a pylorospasm may have disappeared or a cap irritability originally noted may not be in evidence, but the film evidence will be much the same. If, however, a niche has been demonstrated with compression technique used at the original examination, it is now possible with similar technique to obtain much information of healing. The niche may be smaller or may have completely disappeared. Converging mucosal folds may be seen with their central point at the site at which the niche was previously visualized.

Careful roentgenoscopic examination in which manual palpation expresses barium from the bulb will show a large percentage of bulbar niches but with the use of compression when obtaining film studies a niche is occasionally demonstrated which was overlooked roentgenoscopically. The use of local compression in making roentgenograms of a cap is thus not only advantageous in recording evidence of intrinsic pathology, but offers convincing proof of a lesion which may be overlooked roentgenoscopically. This is particularly true of superficial ulcerating lesions.

Some types of acute ulcers will show no spot of greater density consistent with niche evidence but will show, according to Schindler and Forssell, an oval or round pseudo-polypoid defect, the diameter of which may be as small as 1 cm. or as large as 4 cm. The general contour of the cap is usually deformed in these cases, but the deformity is not of a fixed type. None of our cases which presented such defects have been operated upon and we therefore cannot offer definite proof of their presence. In the cases where we were able to demonstrate these defects, we were always able to show niche. The case shown in Figures 12 and 14 was apparently of such a type. The original roentgenograms showed well-defined areas of vacuolation around the niche when mild compression was used. These were too faint to reproduce well in prints. Forssell believes that such defects may be produced by cushions of edematous mucosa, as based on his preoperative roentgen studies and postoperative roentgen anatomical observations of resected duodenal bulbs. Forssell agrees with Åkerlund in that "typical niche shadow is the most reliable ulcer sign, that is, if the niche shadow shows itself as a well defined spot denser than its surroundings and recurring in several roentgenograms. Such a niche

Fig. 24. Large duodenal ulcer niche.

shadow does, in my opinion, not always with certainty correspond to the cavity of the ulcer, but may just as well be some retained sedimentary contents located between abnormally stiff and immovable folds of mucous membrane in the surroundings of the ulcer." When niche shadow is not present Forssell believes that a very suspicious sign of ulcer is "a defect in the bulbar lumen, in the form of a cushion of mucous membrane bulging into the lumen and obstinately persisting for a long time in spite of compression of the bulb." In acute ulcer where the niche is visible, the zone around the visualized niche may present a similar defect. The contour and size of the niche may vary in detailed studies made under varying degrees of compression. Re-examination after a period of medical management may show converging mucous folds as evidence of cicatricial changes incident to healing. Berg designates this appearance as "corona radiata."

Anatomical proof of some of these changes is difficult to obtain as they are usually regarded as medical cases and are not referred to the surgeon. The clearness of niche visualization or the size of an individual niche is of no surgical significance as these frequently completely disappear after six to eight weeks of medical management. Several of our cases showed complete disappearance of niche or crater flaking six weeks after beginning treatment. Several others showed considerable diminution in size at this time. In many of our cases, it was impossible to obtain re-examination.

Many patients will present a deformity of the cap characteristic of duodenal ulcer but no demonstrable niche evidence. In this group it may be said that films made with the cap under compression are of no greater value than those made without local pressure. This is probably a just criticism but one does obtain the assurance that no roentgenographically demonstrable niche is present. Films of the barium-filled cap should, of course, not be omitted, as changes due to extrinsic lesions may be overlooked if only mucosal studies are made.

The use of the word "compression" in speaking of this technique, while properly descriptive as to its meaning, may raise the objection of harmful results because of too great pressure over a diseased structure. The amount of pressure is not great, frequently the mildest degree suffices to distribute the amount of barium necessary to visualize the mucosa. The pressure also is distributed and not of a point type. In one and a half years' experience with this technique, we have seen one patient suffer perforation of a duodenal ulcer a few hours after examination. The ulcer was of a

FIG. 25. Complete stenosis of descending duodenum as a result of pancreatic malignancy.

Fig. 26. Barium-filled cap showing normal contours.

Fig. 27. Same case as shown in Figure 26. Under compression en face niche is shown. The patient had symptoms of an acute ulcer.

penetrating type, and while the local pressure may have hastened perforation, it is likely that the same complication would have occurred with simple palpation of the cap incidental to roentgenoscopic examination, or even if the patient had not been examined.

The accurate interpretation of roentgenograms made with compression technique requires considerable experience. Until thoroughly experienced in the use of compression technique one is apt to be over-enthusiastic in diagnosing niche evidence. Frequently barium is caught in a pocket formed by cicatricial changes and its appearance may resemble a niche, or barium may be caught between mucosal folds and miscalled a niche, although there is a distinct difference in appearance. Differentiation is possible by the use of a series of films with the cap under various degrees of compression.

There are two parts of the duodenal bulb at which pockets frequently occur—the lesser and greater curvature sides of the base. These have been designated by Forssell as the superior and inferior recesses. The diverticular pouches secondary to chronic duodenal ulcers commonly retain barium on compression and one should not be misled into interpreting such a finding as niche. There may of course be pockets in other parts of the cap which will retain barium and mislead one who is inexperienced in this technique.

Most commonly niche evidence is roentgenologically shown on the lesser curvature side and usually on or toward the posterior wall of the bulb. According to post-mortem statistics, the anterior wall ulcer is found more frequently than the posterior wall lesion. Roentgenologically, however, niches of the posterior wall are more commonly seen, probably because these retain barium substance more easily during palpation and compression than those on the anterior wall. Although ulceration is uncommon in the upper portion of the cap and in the descending duodenum, it does occur and one should always obtain a few views with compression centered over these regions.

Ulcer is by far the most commonly encountered lesion in the duodenum, but other types of pathology may be advantageously shown through the use of compression in obtaining roentgenoscopic studies. Pedunculated polypoid tumors may be well demonstrated in a barium-coated cap.

Obstructing lesions in any portion of the duodenum may be more accurately shown on roentgenograms made with compression over the stenotic tract (Fig. 25). Alberti even makes diagnoses of varices of the duodenal bulb by demonstrating certain characteristic mucosal contours on films made under compression. His roentgen studies are interesting but far from convincing. He describes horseshoe-shaped mucosal ridges as characteristic of ectatic veins and reports 3 cases of unexplained hematemesis in which he found what he considered justifiable roentgen evidence of duodenal varices.

SUMMARY

(1) Compression technique as a means of obtaining roentgenographic studies of mucosa in relief is a valuable supplement to roentgen study of the duodenal cap.

(2) It increases the percentage of niche visualization. Evidence of the niche, when present, is shown with a high degree of detail.

(3) Considerable information as to the response of an ulcer to treatment may be obtained when a niche has been visualized.

(4) In a certain small percentage of cases, lesions of the duodenal cap may be demonstrated roentgenographically by the use of this technique which would not be shown by either roentgenoscopic or other roentgenologic methods.

(5) In some types of duodenal ulcer, compression adds no information to that obtained by studies of the barium-filled cap.

(6) Accuracy of technique and interpretation is acquired only after considerable experience with the method.

(7) In this study, compression obtained by the Chaoul compressor was found to be the most satisfactory.

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DISCUSSION OF PAPERS BY DRS. GRIER AND GEYMAN

Dr. Grier (closing). Dr. Geyman's beautiful work is simply another evidence that this method is of the utmost value. This, of course is another method of making plates under roentgenoscopic control. In my paper I refer to this, and although I have not had very much experience with this method, it undoubtedly is a method of making plates under roentgenoscopic control and usually, of course, in the erect posture. Since this is so evident and since Dr. Geyman had this paper on this program, I spent very little time referring to making plates in the erect posture.

Dr. Geyman (closing). With regard to the application of this technique to the stomach, this was not mentioned because compression added nothing to the results obtained with other methods. Penetrating ulcers of the stomach are much better visualized with serial studies after a complete barium meal than with a fractional meal, with or without compression.

The danger of misinterpretation is perhaps the greatest danger in the use of compression technique, and if anything should be stressed this point needs emphasis. Only familiarity with typical niche appearance will avoid diagnostic pitfalls of this method. The other point I wished to mention is the use of compression in the prone position, and I believe this should be condemned. I have never used compression in the prone position after my first experience with the procedure. In attempting to show a small duodenal lesion which was noted roentgenoscopically, too great pressure was used in the prone position and the ulcer perforated two hours after the examination. Fortunately, the immediate operation was followed by uneventful recovery. In the erect position pressure is of mild degree and usually the best films will be obtained with light compression, as one should not entirely obliterate barium from the cap for a nicety of visualization.

In closing, I might again say that this study is presented, not because it is anything revolutionary as a new diagnostic aid but is a valuable supplementary procedure which we have found helpful, not because it materially increases our percentage of accurate diagnoses, but because it gives us information which we could not obtain with other methods.

Dr. William H. Stewart. How about exposure, Doctor?

Dr. Geyman. I mentioned that rather hurriedly. It is very essential, of course, not to use long exposures

Dr. Stewart. I mean to yourself.

Dr. Geyman. I have not been using more than ordinary protection, lead gloves and lead apron. However, only a very small diaphragm opening is used during the exposures as the region under compression is, of course, not more than 3 square inches. Also the fluoroscopic screen is between the cassette and the examiner, which offers considerable protection. It might be wise, however, to make some measurement tests and I shall plan to do this in the near future.

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EXPERIENCES IN INTERSTITIAL IRRADIATION OF CARCINOMA OF THE BREAST

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THE use of interstitial irradiation in carcinoma of the breast is not a new procedure. A perusal of the literature shows that it has been practised for many years, but the technique has changed from time to time. When first introduced it was carried out by means of steel needles containing from 7 to 12 milligrams of radium, and the primary tumor only was surrounded by needles, for no attempt was made to influence the lymph nodes. While effective, the results were not always favorable because of the necrosis produced by the irritating β-radiation; consequently its use became greatly restricted. With the advent of radon in glass seeds this type of irradiation became popular again, but inadequate filtration was followed by necrosis and such prolonged pain that it, too, fell into disuse until gold and platinum seeds were introduced. The use of highly filtered radon enables one to give the required dosages, but it is extremely difficult to be assured of accuracy of distribution in large masses of tissue as found in the breast. Furthermore, in large tumors the item of expense with these seeds is considerable for the average patient.

With the advent of the British School of Radium Research added interest in interstitial irradiation has taken place. The technique evolved and its rationale are based upon principles laid down by Regaud in his biological and radiological studies, and they rest on the following points:

(*a*) Multiple points of radiation accurately placed in the tissue.

(*b*) Use of small amounts of radium salts in platinum needles which have a high filtration value, eliminating the α and β particles.

(*c*) Prolonged irradiation in order to influence the malignant cell at some time during the vulnerable cycle of division.

It is with this method of treatment I wish to present our experiences during the past year.

A careful review of the reports published by Keynes, Cade, Fitzwilliams, Handley and Cheatle shows that there is an apparent attempt to approximate a most radical breast resection by a thorough and constant irradiation of not only the breast tumor but also of those normal parts that may harbor the advancing edge of the growth, as well as those regions into which the lymph channels drain. This immediately places the procedure on a surgical rather than a medical basis as is found when surface irradiation is practised. Therefore, the principles of strict surgical asepsis must be carried out and an accurate knowledge of anatomical structures must be had by the operator to avoid doing damage to vital structures. The breast and the pectoral muscles may be pierced by needles with impunity, but in axillary and supraclavicular regions, as well as the internal mammary area, care must be exercised when needles are inserted because of the important vessels which, if punctured, may lead to a fatal hemorrhage.

TECHNIQUE

In the main, our technique is similar to that used by Keynes, Cade and Fitzwilliams, and was described by my colleague, Costolow, in 1930. The needles are plunged through a stab wound made in the skin by a sharp-pointed scalpel, and are placed at intervals of from 1.5 to 2 centimeters, in such numbers as to attain a "radium Halsted." Obviously it is not possible to lay down any definite rules concerning the actual number necessary to attain this, since the size of the individual, the breast, and the other involved tissues must be the determining factors. Each needle has an

anchoring cord of waxed silk on which is fastened a colored bead which immediately tells us the amount of radium in that particular needle. Along the waxed cord is placed a loop through which a suture of plain catgut is passed, anchoring it to the skin, so that at the end of from seven to ten days when the needle is to be removed the catgut is digested and a gentle pull on the silk easily removes the needle. All of our needles have a filtration of 0.5 millimeter of platinum and their distribution is as follows:

A. *Around the Tumor.* The needles used in this region are 4.4 cm. long and each contains 2 mg. of radium. They are passed around and underneath the tumor where it is attached to the fascia and pectoralis major muscle. As these are plunged from all sides it is seen that the center of the tumor on its posterior surface is subjected to a great deal of crossfire. Beyond the primary row a second row of shorter needles, 2.8 cm. long and of 2 mg. capacity is placed. Occasionally, if the tumor is very large, a few needles are placed within the circle of long needles so as to lie between the skin and the tumor. Previous workers make mention of the fact that some needles are plunged directly into the tumor mass itself. We have attempted to do this but have never been successful, since the growth is of such cartilaginous hardness that platinum needles cannot be pushed in without danger of breaking or bending. For this reason we have contented ourselves with surrounding the tumor completely.

B. *The Axilla.* Since this area is usually the seat of the earliest extension, three or four needles 4.4 cm. long, and containing 2 mg., are inserted into the apex of the axilla. To prevent any accidental injury of important structures they are inserted parallel to the vessels, but if a node or a group of nodes is palpable an attempt is made to surround them by needles; this gives a thorough crossfire to palpable evidence of the disease.

C. *Subpectoral Area.* This region is between the pectoralis major muscle and the chest wall, and contains the lymphatic vessels running from the breast into the axilla. Needles 2.8 cm. long and of 2 mg. each are placed along the lateral border underneath the muscle.

D. *Posterior Axillary Line.* As some lymph vessels are found in this region, running up to the axilla, a few needles 2.8 cm. long and containing 1.3 mg. are inserted.

E. *Costocoracoid Region.* This is really the extreme apex of the axilla and contains nodes along the subclavian vessels just below the clavicle. Needles are plunged through the clavicular portion of the pectoralis major and its fascia to reach these nodes. They are 2.8 cm. long and contain 2 mg. of radium.

F. *Supraclavicular Region.* The posterior cervical triangle is often the seat of malignant extension through its nodes, therefore needles are placed parallel to the clavicle and posterior to the sternocleidomastoid muscle. They are 2.8 cm. long and contain 1.3 mg. of radium. As these needles are usually directly under the skin, less of the radium is used in each needle.

G. *Internal Mammary Region.* Since the nodes in the intercostal spaces along the internal mammary vessels are infected comparatively early in some patients, needles 2.8 cm. long and containing 2 mg. of radium, are plunged into the first four interspaces 0.5 cm. external to the edge of the sternum, so that the point lies posterior to and underneath the sternum.

ANESTHESIA

We have used both general and local anesthesia for this work. Nitrous oxide and oxygen are very satisfactory, but we are now relying more and more on $\frac{1}{4}$ grain of morphine and 1/100 grain of hyoscine hypodermically. This is supplemented by a small amount of novocaine (1 per cent) at the puncture points. Patients do not complain, and the anesthesia is satisfactory, though it does take a little more time than under a general anesthetic.

COMPLICATIONS AND REACTIONS

No serious complications have arisen. The danger of passing a needle in blindly along the axillary vessels and in the intercostal spaces underneath the sternum is constantly borne in mind. Serious hemorrhage or pneumothorax may result, but we have had no difficulty, although occasionally if bleeding persists and is due to the puncture of a small vein not controlled by pressure, a ligature is used. During the time when the needles are in place the puncture point may become infected, and if so, after the needle is removed healing is delayed. As was mentioned earlier, only strict adherence to surgical principles can prevent this.

The first few days may be followed by considerable soreness in the axilla and along the mammary punctures, due to contractions of the pectoralis major muscle. However, if the patient holds the arm still, the pain is not marked. There is usually a slight rise of temperature up to 100° F. for a few days, which subsides in three or four days. In addition, the patient may experience a little nausea but otherwise there is no constitutional disturbance.

Locally, the breast and surrounding tissues become somewhat edematous about the fourth day. This edema is of the boggy variety and gradually increases until the needles are removed. When this is done a drop of *Staphylococcus albus* pus appears at the puncture point, and the skin surrounding each one is erythematous over an area 1 cm. in diameter. In about two weeks the skin over the tumor and in the axilla assumes a marked erythema and if the irradiation has been thorough it is followed by a desquamation, leaving a raw red base covered with lymph. It heals gradually after two or three weeks. In about six weeks the reaction in the skin has entirely gone but a doughy edema remains in the breast itself. The skin may slowly change its color and in from four to six months there is moderate pigmentation. The mass in the breast which first enlarges, becomes softer, shrinks slowly and in six months nothing palpable remains except some scar tissue or a small firm mass that is freely movable and not tender. In patients where the tumor was adherent to the skin this attachment has loosened and movement becomes unrestricted. At the end of from six to eight months some patients complain of a pulling or drawing sensation as well as an aching sensation. This has been described as a neuritis and is in the nature of complaints suffered by patients who have had interstitial irradiation from radon in other parts of the body, notably the neck.

EFFECTS ON THE BLOOD

With such a prolonged irradiation, one would expect a marked variation in the blood picture. The hemoglobin and erythrocytes show no great change; if anything, they are both increased. This may possibly be due to concentration of the blood from dehydration. The leucocyte count does, however, show a drop of from 1,500 to 2,000. The greatest fall is in the lymphocytes, with a proportional increase in the neutrophiles. This increase of the polymorphonuclears may be only relative, since prolonged surface irradiation gives about the same findings. However, there have been no permanent ill effects, inasmuch as normal readings are usually found in about eight weeks.

CASE REPORTS

As this type of treatment is more or less experimental, it is wise to group the cases for purposes of comparison and study. Three series have been under observation.

Group I. Operable—patients who refuse removal of the breast, or whose physical condition precludes operation.

Group II. Inoperable.

Group III. Recurrent—postoperative.

Illustrative case reports under each are taken up separately and discussed.

Group I. Operable.

CASE I. Mrs. B., aged seventy-two. First seen March 31, 1930.

Diagnosis: Carcinoma left breast.

Two months before the patient reported to us she had accidentally noticed a small lump in the left breast which gradually increased in size, but there has been no pain at any time. For many years she has had cardiac symptoms associated with a blood pressure of 200 mm. Hg, and a great deal of dizziness.

Examination shows a fixed mass 6 cm. in diameter in the upper outer quadrant of the left breast. The skin is adherent and retracted, while fixation to the muscle is very marked. There is a firm, fixed gland in the left axilla.

Treatment: On March 31, 36 needles containing 67.8 mg. of radium were inserted into the breast and surrounding structures. On April 8, they were removed, giving a dosage of 12,797 mg-hr.

Supplemental Treatment: On May 24, high voltage roentgen rays, 165 kv., constant potential, 4 ma., 50 cm. distance, 1 mm. Cu and 1 mm. Al filter, 60 minutes over left breast anteriorly. On July 5, the above dose was repeated.

Results: Moderate reaction only. On January 22, 1931, a palpable nodule 2.5 cm. wide remains. The patient's general condition is good but she should be re-needled and if her condition permitted surgery, a simple excision might be advisable.

Case II. Mrs. B., aged forty-eight. First seen May 16, 1930.

Diagnosis: a. Carcinoma left breast. b. Fibroid uterus.

History: Six months ago she noticed a lump in left breast. No pain at any time. Has also had profuse menses with a persistent menorrhagia for six weeks.

Examination: Large, hard, irregular mass in left breast 8 cm. in diameter, fixed to skin and fascia. Two or three firmly fixed glands in the left axilla. Pelvic examination reveals a uterine fundus which is nodular and enlarged to three times normal size.

Treatment: On May 26, 44 needles containing 76.8 mg. of radium were inserted into the left breast and the surrounding tissues. They were removed on June 2 and June 5, giving a total dosage of 17,875 mg-hr.

Supplemental Treatment: On May 21, high voltage roentgen rays, 165 kv., 4 ma., 1 mm. Cu and 1 mm. Al filter, 50 cm. distance, 30 min. over the left breast. There was also a pelvic cycle given to control the menorrhagia from the fibroid uterus.

Results: The reaction was quite marked; the skin peeled off and the mass became softer. In November there was no palpable evidence of disease, but in December the patient reported with a painful mass in the axilla which had the appearance of an infection. This gradually subsided and patient is now in good condition.

Case III. Mrs. B., aged fifty-one. First seen September 12, 1930.

Diagnosis: Carcinoma right breast with axillary involvement.

History: Six months ago noticed lump in right breast which has been treated by lights.

Examination: Firm nodular mass 5 by 6 cm. in upper half of right breast. A small movable gland is palpable in the axilla.

Treatment: On October 7, 42 needles containing 75.6 mg. of radium were inserted. These were removed on October 16, giving a total dosage of 16,330 mg-hr.

Preliminary Treatment: High voltage roentgen rays, 165 kv., 4 ma., 50 cm. distance, 1 mm. Cu and 1 mm. Al filter, applied over right breast and axilla from September 13 to 22.

Result: A severe reaction took place. There was a complete denudation of the skin over the breast which healed in a month. When examined in December there was no palpable evidence of disease.

Case IV. Mrs. H., aged fifty. First seen July 17, 1930.

Diagnosis: Carcinoma right breast with axillary involvement.

History: Had what was called a Paget's disease of the right nipple three years ago. This healed under surface irradiation, but she noticed a lump in the right breast two months ago. There is no pain.

Examination: Hard, fixed mass in right breast 6 by 7 cm. The skin is not adherent but the nipple is retracted, and in the axilla are found a few glands of rubbery consistence.

Treatment: On September 4, 1930, 42 needles containing 72 mg. of radium were implanted. These were removed eight days later, giving a dosage of 13,824 mg-hr.

Preliminary Treatment: High voltage roentgen-ray cycle to the breast in July and August, 1930.

Result: There was a strong reaction with desquamation, and in March, 1931, there was no palpable evidence of disease.

Case V. Mrs. D., aged forty-nine. First seen in May, 1930.

Diagnosis: Carcinoma right breast.

Complaint: Four years ago noticed a lump in the right breast which has grown gradually. There is no other complaint except for neuritis(?).

Examination: Patient is well nourished. A fixed, hard mass in the upper half of right breast is palpable. It is 10 cm. in diameter and adherent to the pectoral muscle over the third and fourth ribs, and the skin is attached to it over an area 2.5 by 2.5 cm. No glands are found.

Preliminary Treatment: June 4, 1930—Radium pack 6×6×3 cm., with 100 mg., filtered through 1 mm. of brass, applied for forty-eight hours; dosage 4,800 mg-hr.

Treatment: August 22, 1930, 33 needles containing 63.9 mg. inserted around tumor and surrounding structures, giving a total dosage of 13,792 mg-hr.

Result: A severe reaction took place with complete disappearance of the growth. There is no fixation and the skin has lost some of its pigment in the treated area.

Group II. Inoperable.

CASE VI. Miss McN., aged thirty-nine. First seen in November, 1929.

Diagnosis: Carcinoma right breast with axillary involvement.

History: One year ago patient noticed a lump in her right breast which has grown gradually, but is painless. She has had high voltage roentgen therapy to the primary tumor as well as to both axillary regions, but there is no change.

Examination: Hard, irregular mass 6 by 8 cm. in upper outer quadrant of the right breast. There are a few small firm glands in both the right and left axillary areas.

Treatment: On May 14, 44 needles containing 76.7 mg. of radium were inserted; removed May 24 after a total dosage of 18,408 mg-hr.

Result: Severe reaction with desquamation of the skin over the tumor. The mass in the breast became softer and smaller, while the glands decreased in size. In July she developed a marked shortness of breath, but nothing was found except a paroxysmal tachycardia, although metastases were suspected. Patient died in September, apparently from some cardiac disturbance. The blood examination six weeks before her death revealed 80 per cent hemoglobin, 5,000,000 red blood cells, 6,020 white blood cells, 67 per cent polymorphonuclears, 15 per cent small lymphocytes, 9 per cent large lymphocytes, and 9 per cent transitionals.

Group III. Recurrent—postoperative.

CASE VII. Mrs. V., aged forty-two.

Diagnosis: Postoperative recurrence left supraclavicular gland.

In 1925, the patient had the left breast and axillary glands removed for a scirrhous carcinoma. In 1929 there was a return in the supraclavicular glands and she was given a course of high voltage roentgen therapy, followed by radium pack, with some improvement. In May, 1930, however, there was a further increase in activity.

Examination: The operative wound is well healed. No local pathology except for numerous fixed glands above the left clavicle.

Treatment: On May 20, 1930, four 1 mg. needles were plunged around the glands and left in for ten days, with a total dosage of 960 mg-hr. On October 21, 1930, eleven 1 mg. needles were plunged around the new glands with a total dosage of 1,728 mg-hr.

Result: There was considerable reaction, resulting in the disappearance of the glands.

ADVANTAGES AND DISADVANTAGES

No new method of treatment should be advised without considering its advantages and disadvantages. To our minds it seems that the *advantages* lie in these points.

(*a*) Simplicity of execution. If anatomical factors are borne in mind so that accidental injury is avoided, it appears that this method of attacking carcinoma is ideal, since there is no shock in carrying out the operative procedure.

(*b*) It can be used in inoperable cases. The inoperability consists only in advancement to the supraclavicular area. If there is bony involvement it is obvious that this treatment which, like surgery, is purely local, will have no effect on distant metastasis.

(*c*) Ability to influence the supraclavicular and mammary group of lymph nodes. Although these glands may be removed surgically, the chances of success are poor, while the shock of the prolonged operation is very great.

(*d*) No mutilation of the normal struc-

tures, consequently no interference with function.

(*e*) Ability to repeat the treatment if necessary, and if need be, a small residual lesion may be removed from the breast itself.

The disadvantages are as follows:

(*a*) There is no way of knowing whether one is dealing with carcinoma unless a biopsy is performed. This is necessary for statistical purposes, but clinically most advanced cases can be diagnosed correctly.

(*b*) There is no way of knowing whether the irradiation has reached all structures that may be the seat of malignant extension. This same disadvantage is applicable to surgery.

(*c*) The residual discomfort, which consists of a dull aching pain described as neuritis. Whether this is worse than the edema and discomfort seen after removal of the muscles and fascia after the radical operation remains to be seen.

(*d*) Occasionally it is necessary to repeat the treatment. Recurrence is frequent after operation so that this is not a valid excuse.

DISCUSSION

Inasmuch as our work is based mainly on a clinical diagnosis of carcinoma it has little statistical value. Only the cases recurrent after operation have a pathological diagnosis, though all the other patients fulfill the criteria for a clinical diagnosis of carcinoma. It is interesting, however, to note the effect of irradiation used in this manner, and to see how effective it is on glandular infiltration as well as on the primary tumors. Though it may be inferior to surgery in the operable group at present, its initial and lasting effects in the inoperable group are superior to surgery and surface irradiation. In the meantime, one should proceed slowly and draw no conclusions until patients have been under observation for a number of years. However, the primary results are exceedingly favorable for a more extensive study of this method, and indications point to the fact that we have a method which will accomplish what radical surgery attempts to do, but without its deformity and its surgical shock.

NOTE: July, 1932. Case I had a recurrence in 1932 and following a mastectomy she died from the cardiac condition.

Case II is well but has a palpable mass.

Cases III, IV and V show no palpable disease.

Case VII is living but has recurrence around the operative scar for which she has been receiving surface irradiation at the California Institute of Technology.

Vol. XXVIII, No. 2

TREATMENT OF CARCINOMA OF THE ESOPHAGUS WITH RADON IMPLANTS

A DESCRIPTION OF AN IMPROVED IMPLANTER

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THE esophagus ranks next to the uterus, breast and stomach as a site for which cancer has a predilection, about 0.5 per cent of all malignancies occurring there. The middle third is most frequently involved, the lower third next and the upper third least often. Their relative frequency may be expressed by the numerals 3-2-1. Men are affected four to five times as often as women and most frequently in the fifth decade of life. The natural constrictions of the esophagus are the usual locations for the beginning of a malignancy, but other parts are often involved. The tumor may infiltrate the entire circumference of the esophagus, causing an annular narrowing of the lumen, or may protrude as a bulky mass into the lumen.

Histologically, squamous-cell carcinoma is the type usually found in malignancies of the esophagus, but occasionally cylindrical or adenocarcinoma is present in tumors involving the lower portion of the esophagus.

The origin of the adenomatous type is assigned to the numerous small islands of mucous glands 2 to 10 mm. in diameter scattered through the upper part of the esophagus and to a lesser extent in the lower part. These glands are of the branched tubular type, lined with cylindrical cells, secrete mucus and resemble the glands of the stomach. Nevertheless, the adenomatous type of carcinoma is rarely present where these glands are most numerous. Small rudimentary canals present in the submucous and muscular layers of the esophagus, as a result of an incomplete separation of the esophagus and trachea at an early embryonal period, have also been thought to be another site where epithelial hyperplasia and malignancy originate. In many cases the lesions situated at the lower end of the esophagus have proved to be an extension of a malignancy involving the cardiac end of the stomach.

Esophageal tumors are usually slow-growing, histologically not very malignant, metastasize late and cause little discomfort until ulceration or increase in size of the tumor actually interferes with the passage of food, on account of spasm or blockage of the lumen. The patient is usually in good health until such time as the tumor has reached sufficient size to render swallowing painful. Then the patient begins to lose weight from undernourishment. The earliest sign, however, is the feeling of a slight pain on swallowing and the sensation of having a lump behind the sternum. Unfortunately, the lesion in the very early stages is not easily recognized roentgenoscopically and when in such cases an examination proves negative, especially for aneurysm, mediastinal tumor, substernal thyroid and other extrinsic causes for pressure on the esophagus, and the pain on swallowing still persists, an esophagoscopic examination should be made. Esophagoscopy, however, is still used by many as a confirmatory rather than as a primary diagnostic procedure. It is for this reason and in spite of education and propaganda relative to the symptoms of incipient carcinoma of the esophagus, that the patients whom we see in clinics and private practice are usually in the advanced stages of the disease, when marked dysphagia and actual obstruction have directed attention to the esophagus.

Surgical removal of a localized esopha-

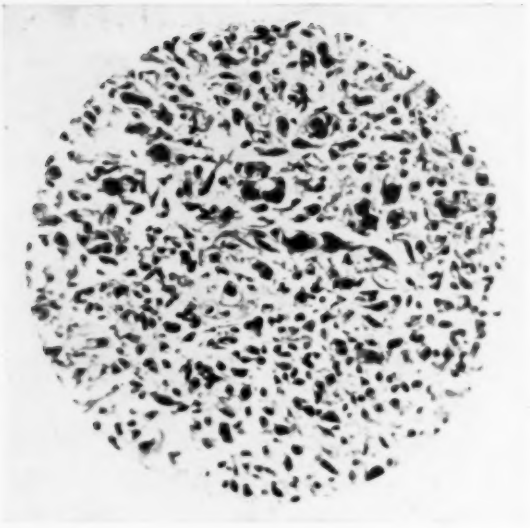

Fig. 1. Squamous-cell carcinoma of the esophagus. This is the usual type malignancy in the esophagus. Note the presence of many hyperchromatic transitional cells.

geal lesion has been advocated by Jackson and others, but the lesion is rarely discovered sufficiently early to render possible its removal with any probability of success. Jackson, in speaking of the surgical possibilities states: "Here we have a local process of a relatively low degree of malignancy; it is reasonable to expect a good percentage of cure if the surgeon could get the patient in this stage, but he never does and never will, so long as present obsolete diagnostic methods are taught to the profession." The literature records 5 cases who have successfully weathered the initial surgical procedure. Torek's case lived twelve years but the others succumbed within a few months. With improved surgical technique and early diagnosis, the number of successful cases would undoubtedly be increased, but until the time comes when surgeons will be able to duplicate the single success of Torek, we must bend all effort to treat the patient when he comes to us, in a manner that will offer him the greatest possible relief, no matter what the condition of the lesion may be.

Gastrostomy is advocated by many as a palliative measure for maintaining body nutrition and putting the esophagus at rest. The pain behind the sternum is relieved to a considerable extent by the diminution in the accompanying swelling of the tumor, when the trauma of passing food is removed from the esophagus. Gastrostomy must be performed early in the disease while the patient is still in comparatively good physical condition. If performed late, it is of little or no value.

Esophageal intubation, as a substitute for gastrostomy, is preferred by some workers. This procedure requires bougienage and stretching of the constricted part of the esophagus under direct esophagoscopic observation, and when the lumen of the esophagus, through the tumor area, has been stretched to 1 cm. or more, a rubber or German silver tube is inserted and left in situ. The funnel-shaped upper end of the tube keeps it from slipping downward, preventing the further contraction or stricture of the esophagus and permitting the free passage of food to the stomach. The tube remains in place until the patient dies, which may occur in a few weeks or months following the intubation.

Neither of the above surgical procedures, although necessary adjuvants in the treatment of the patient, attacks the primary

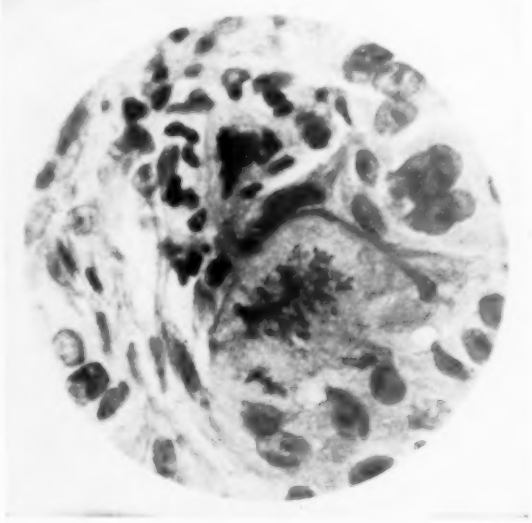

Fig. 2. Squamous-cell carcinoma. High magnification of same section. Note cell undergoing mitosis.

lesion, which eventually proves fatal in a short time.

Radiation, likewise, has offered little in the way of cure, for the reasons that the lesions are usually discovered late, the wall of the esophagus is normally very thin and elastic and often the entire thickness of the esophageal wall is involved by the tumor. Many vital structures are in intimate anatomic relation with the esophagus. At times a tumor may have actually extended to and involved an adjacent organ and the application of radiation will sometimes destroy the tumor cells which form the very barrier between two important structures. Accidents in the treatment of malignancy of the esophagus are therefore frequent, and fistulous formation leading to trachea, bronchus, lung, pericardium and the perforation of the aorta are not uncommon. With early diagnosis and proper irradiation these accidents might be minimized.

Because the results by any method are discouraging, the treatment of carcinoma of the esophagus has been approached with the idea of palliation and relief of symptoms rather than the cure or arrest of the initial lesion. Nevertheless, cases have been reported where patients have lived two three, five, and one case even eleven years, after radium treatment with complete disappearance of the tumor.

Fig. 4. J. S. Roentgenogram of an annular carcinoma of the middle third of the esophagus. Histologically proved to be squamous-cell. Note the size of the canal through the tumor ⅛ inch in diameter. The upper part of the esophagus is wider than the lower portion. Radon seeds implanted interstitially on December 5, 1930. Total dose 2,500 millicurie-hours.

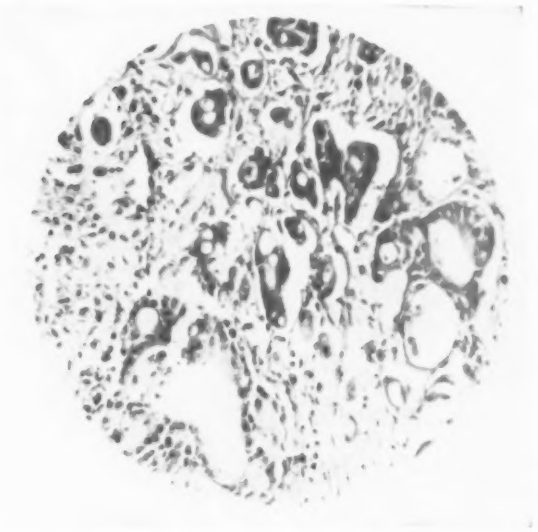

Fig. 3. Adenocarcinoma. A rare type in the esophagus and usually present in the lower third. Note the atypical formation of glandular elements and the infiltration of the stroma.

Various methods for the application of radium have been used:

1. Interstitial irradiation by the implantation directly into the tumor mass of gold or platinum removable or permanent capillary tubes containing radon.

2. Intraesophageal irradiation by the passage of radium containing tubes, either singly or in chains, down the esophagus and through the constricted lumen of the tumor-bearing portion and permitting the radium to remain in the vicinity of the tumor until the desired dose is administered. This dose may be given in one or more applications.

Fig. 5. Roentgenogram of same patient as in Figure 4 taken March 11, 1931, three months after radon implantation, showing the effects of radiation on the tumor. The lumen has widened to ¾ inch in diameter. Patient is able to take liquids and soft solids and has gained 15 lb. in weight. No gastrostomy was performed. Radon seeds are visible in the wall of the esophagus.

3. External irradiation by the application of a radium pack to the surface of the body opposite the tumor.

At the Curie Institute in Paris, Regaud has had unusual success in the irradiation of tumors in general by following certain established principles. These are: (1) that small amounts of radium over longer periods of time give better biological results than larger amounts of radium applied over a short period of time; (2) that all parts of the tumor, especially the base, must be irradiated equally, and (3) that crossfire irradiation accomplishes better results than direct irradiation.

To scrutinize the various methods of irradiation heretofore used, in the light of the above criteria, we must first get an eye picture of the tumor as the operator, who is about to use radium, sees it. The general size of the tumor, the diameter of the lumen through the tumor, whether or not it is annular, and its location in the esophagus is determined from a roentgen study of the esophagus and from an esophagoscopic examination. The required total irradiation is next determined by estimating the cubic capacity of the tumor and its relative radiosensitivity as obtained from a histologic study of a section of the tumor. Approximately 130 millicurie-hours of radiation per cubic centimeter of tumor tissue is usually required to effect a destruction of the malignant cells.

When treating the lesion, the radiologist sees the tumor through the esophagoscope. He sees only the top or proximal end of the tumor and the opening of the narrow lumen of the esophagus passing through it, but rarely, if ever, does he see any part of the tumor distally. He proceeds to implant the seeds or needles into the top and visible surface of the tumor, using the straight implanter. To reach the distal parts of the tumor he passes the implanter down the narrowed esophageal lumen and attempts to imbed the seeds into the sides of the tumor mass. Here he meets with considerable difficulty for he cannot twist or point the end of the implanter to one side or the other and cause it to enter the tumor mass. Partial success is sometimes obtained by getting a long curve into the implanter, but this is a difficult task at a distance of from 10 to 24 inches from the mouth of the patient, when working through a narrow esophagoscopic tube. In the implantation

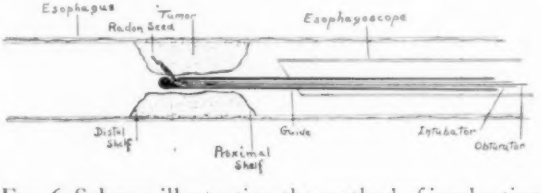

Fig. 6. Schema illustrating the method of implanting radon seeds into the walls of an annular carcinoma of the esophagus. The cross-section is that of an esophagus with the patient in the dorsal recumbent position. Implantation is begun at the most distal portion of the tumor, the first seed being inserted 0.5 cm. proximal to the distal shelf and subsequent seeds at distances of 1 cm.

of additional seeds, the entire implanter is removed and another loaded implanter is used to place each succeeding seed until the desired number have been inserted. There is no guide, but judgment, that can be used in the distribution of the seeds into the tumor mass by this method. Those who have taken the trouble to roentgenograph their patients within a few minutes after such an implantation to determine the location of the seeds are surprised to find that most of the seeds are grouped close together, one or two a little farther away, while others are in the esophagus at a considerable distance from the tumor site, indicating that the latter seeds were laid on the surface of the canal and not imbedded in the mass. The tumor mass therefore does not receive sufficient equalized radiation throughout, as the distribution of the radon seeds or needles is unequal, and it is this inability to properly distribute the seeds that has resulted in a concentration of radiation in the upper part of the tumor which is visible and accessible, thereby causing a subsequent sloughing, perforation and mediastinitis.

With the method whereby a tube or tubes of radium are placed in the lumen against the sides of the tumor under roentgenoscopic guidance, there are several fallacies. The tube in the great majority of cases is not where we think it is, but usually remains on the shelf formed by the upper part of the tumor. Where a gastrostomy had been previously performed and strings attached to both ends of the tube or tubes, one being pulled through the gastrostomy opening, the chances are better for the proper placement of radium within the lumen of the tumor, but then again, it is doubtful if the tubes remain in the same position for one, two or more days. The amount of radiation required to effect the destruction of a tumor by this method is at least three times the amount necessary by the interstitial method. Radiation applied in this manner is also unequal, in that the outer portions of the tumor receive only a fraction of the amount administered to the surface of the tumor, which is directly in contact with the radium tubes, even though heavy filtration is used. The average dose administered by this method, as reported in the literature, appears to have been inadequate to accomplish the desired purpose.

The method of external application of radium by a pack requires a very large amount of the element such as is possessed by very few. The dose required is very large, because of the distance of the pack from the tumor.

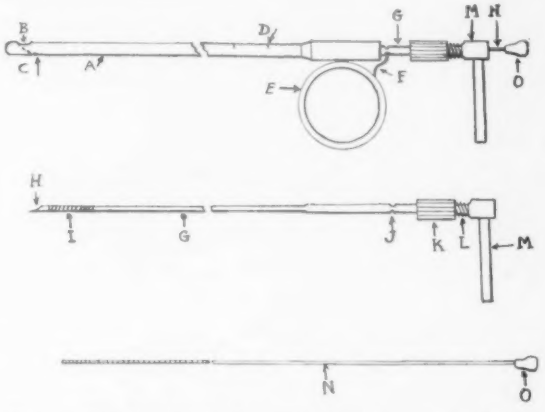

Fig. 7. Esophageal radon seed implanter. *A*—Guide. *B*—Opening in head. *C*—Grooved inclined plane leading to side opening. *D*—Calibrations in cm. *E*—Ring to accommodate middle finger. *F*—Flat spring. *G*—Implanter proper. *H*—Hollow needle tip. *I*—Flexible portion. *J*—Niche, when in contact with spring on guide, indicates that the position of the tip is on the inclined plane ready to emerge. *K*—Collar, regulates the amount of protrusion of the tip through opening in head of guide. *L*—Thread on which collar moves. *M*—Handle. *N*—Obturator or stylet. *O*—Knob.

Of the three methods of irradiation just described, the interstitial method is the method of choice, provided we can distribute the seeds with some degree of regularity, for we would then have small amounts of radium, acting over a long period of time, and because of their distribution have a crossfire effect on the intervening tissue, thus complying with the fundamental principles laid down by Regaud.

In an endeavor to obtain such an equal distribution of radiation, an improved

radon seed implanter has been devised. With this instrument, seeds can be implanted at an angle into the sides of every part of the tumor, including even the most distal portions, with a degree of accuracy heretofore not obtainable. The instrument consists of three parts: the guide, the implanter and the obturator or stylet.

The guide is a long brass tube 3/16 inch in diameter. It is tipped by a solid piece of steel which has an opening at its side. The lumen of the brass tube connects with the side opening of the tip by a curved channel, which forms an angle of 35° with the horizontal at the point of junction on the surface. There is a ring at the proximal end of the tube placed on the surface opposite the opening in the tip, to accommodate the middle finger. The proximal end of the tube is calibrated in centimeters. A small flat spring is attached to the ring for the purpose of engaging a niche on the implanter.

The implanter consists of a long, thin, hollow brass tube 3/32 inch in diameter the tip of which is made of steel and bevelled to a point, so that it may be used as a cutting edge. The proximal end has a short vertical handle 1 inch long, which may be manipulated by the thumb and index finger. The implanter fits into the lumen of the guide and when pushed in fully, will cause the tip to protrude through the side opening in the head of the guide at an angle of 35°. The amount of protrusion is regulated by a threaded collar at the proximal end of the implanter. There is a niche on the proximal end of the implanter, which when engaged by the spring on the guide, indicates that the tip of the implanter is just below the side opening in the head of the guide.

The obturator or stylet is a thin piano wire with a flexible tip, which fits into the lumen of the implanter. A knob is attached to the proximal end of the wire. When the obturator is fully engaged the tip protrudes 1/64 inch beyond the point of the implanter.

Technique of Implantation. With the patient in the dorsal recumbent position, the esophagoscope is passed down the esophagus. The guide is passed through the esophagoscope down to the proximal end of the tumor. Knowing the length of the tumor, from previous roentgen study, the guide is passed down the narrowed esophageal lumen for a distance slightly greater than the length of the tumor. To prove the position, the implanter is inserted and the tip is carefully protruded. If no resistance is encountered, the entire instrument is slowly withdrawn until the protruding tip of the implanter is arrested. This marks the distal end of the tumor. The implanter is then withdrawn into the sheath of the guide and the latter is withdrawn a distance of 0.5 cm. An implanter carrying a radon seed in its tip is then pushed down as far as it will go, causing the tip to emerge through the side opening in the tip of the guide and pierce the tumor mass. The obturator is then pushed down propelling the radon seed into the tumor. The implanter and obturator are then withdrawn, but the guide is permitted to remain in place. This is important. The guide is then rotated 90° or 120° depending upon whether four or three seeds are to be implanted at that level, in a circle. The position of the opening in the head of the guide is always known because it is opposite the finger eyelet at the proximal end. Subsequent seeds are implanted in the same manner, always rotating the guide after each insertion. When the guide is returned to its starting point, it is withdrawn 1 cm., and additional seeds are implanted at that level. This operation is repeated at intervals of 1 cm. until the entire length of the tumor is covered. The ordinary straight implanter may then be employed to implant the seeds in the proximal shelf of the tumor, placing the seeds preferably at the peripheral rim. This is the only part of the tumor where direct observation is possible. The seeds used each contain 1 mc. of radon.

By this method of implantation, I believe that one can come closer to obtaining the biological effects in conformity with the

principles of Regaud, for we have radon implants piercing the thickness of the tumor at intervals of 1 cm. in the horizontal and vertical planes, thus securing an equalized radiation and a crossfire effect over a long period of time.

In addition, each patient receives a course of high voltage roentgen therapy, using the factors 200 kv., 4 ma., 50 cm. distance, 0.5 mm. Cu and 1 mm. Al filtration, and the anterior and posterior, right and left obliques as four portals.

What the ultimate results will be towards securing a cure by actually destroying the lesion depends in a large measure upon early diagnosis. Chevalier Jackson's words regarding surgical possibilities might well be repeated here for irradiation, and when the profession can be taught to discover malignancies of the esophagus while the lesion is still a local one, actual cure by proper irradiation will be in sight.

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THE CHANGE IN QUALITY OF ROENTGEN RAYS ON PASSING THROUGH TISSUE*

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THE "softening" of roentgen rays, or their increase in wave length upon passing through any scattering substance, elucidated a few years ago by Compton, is now a well-known phenomenon. It is evident that, on account of this property of radiation, a beam of rays having a certain quality when it leaves the roentgen tube, may have quite a different quality within tissue, due to the repeated scatterings of the rays by the substance being traversed. Up to the present time, however, little attention has been paid to the possible effect of this transformation in radiation therapy. Such measurements of quality as have been made refer to the beam as it leaves the tube holder, in air. The use of increasingly harder radiations has been advocated, in general, not so much from any idea of intrinsic advantage in short wave lengths as such, but rather from the knowledge that greater depth doses could be obtained by this means. In fact, it has been quite generally believed that a given quantity of radiation arriving at a given group of cells within a given time would produce the same degree of change in them, irrespective of the quality. This seemed to be borne out by certain biological experiments in which a given number of roentgens produced a given effect, regardless of whether the energy was delivered by hard or soft roentgen rays.[1] More recent experiments, however, have shown that to produce some different specific biological effects, different quantities of radiation are required in the form of gamma rays from those which are necessary when roentgen rays are used. The ratio of these two quantities is quite different for some of the various effects studied.[2]

For simple biological media, such as drosophila eggs, the quality of the radiation as measured in air is essentially the same as that producing the effect. But with media involving the use of larger masses of matter, and with clinical phenomena, this is not true. In such cases, in order to obtain definite data regarding the relative efficiencies of various types of radiation, it is necessary to devise some method for measuring the quality of the radiation at the point where the effect is actually being produced, rather than in air before it reaches the medium. Determination of the quality in air after the rays have passed through a slab of scattering material and issued on the other side will not serve the same purpose, for the proportion of scattered radiation in that case would be quite different from what it would be within the mass. The depth within the substance is important, as is also the volume irradiated, for both affect the amount of scattering. It is evident that the quality will vary from point to point within the medium, being at all points different from that in air. For a heterogeneous beam of rays, such as is used in therapy, calculation of these changes in quality would be very difficult. The only way to study them is to devise an instrument by means of which quality can be determined at the point in question.

Quality, in general, is determined from absorption curves made by interposing filters in the path of the rays and measuring successive decreases in ionization. It may be expressed by stating the absorption coefficient, the half-value layer (thickness of copper or other filter necessary to reduce the ionization to 50 per cent of its initial value), or the effective wave length (the wave length of a homogeneous beam of radiation which would be absorbed in the same manner in a given filter as the radia-

* Read at the Thirty-second Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 22–25, 1931.

tion under observation).[3] In order to determine quality at a depth in tissue, it would be necessary to take an absorption curve at that place. It is therefore necessary in some manner to introduce the ionization chamber and filters directly into the material to be studied. In this case it is evident that the filter must completely surround the chamber, since rays enter it from all directions. The arrangement shown in Figure 1 was devised by Dr. Failla for this purpose. The ionization chamber, constructed from a ping-pong ball, is on the end of a long, flexible cable. The filters are spun hemispherical shells of copper of various thicknesses, which, in pairs, completely enclose the chamber. By adding successive shells an absorption curve can be determined for radiation reaching the chamber under various experimental conditions. It may be supported in air, to determine the quality of the beam as it leaves the tube, or it may be used at the surface or in the depth of the phantom. This particular instrument, having been designed for preliminary tests of the method, was not water-tight and therefore was used mainly with a paraffin phantom. A certain amount of data, however, was actually obtained with tissue. The disc-shaped blocks of paraffin forming the phantom were 28 cm. in diameter and 3.3 cm. thick. In two of them grooves were made which were nearly the size and shape of the chamber and cable, so as to leave only very small air spaces.

For a given beam of radiation, an absorption curve was first made with the ionization chamber supported in air, with no scattering material within several centimeters of it. The second curve was made with the chamber resting in one of the paraffin blocks, with two others beneath it. This would correspond to radiation at the surface of the body. The third was taken with three blocks above as well as three below the chamber, corresponding to radiation at a depth of approximately 10 cm. in tissue. All ionization measurements were made with Dr. Failla's vacuum tube instrument. All curves taken either in air or with the paraffin phantom were repeated several times, good agreement being always obtained.

The first tests were made with radiation at 200 kv. (peak) with a filter of 0.5 mm. copper, since this is the type of radiation most commonly used at present in deep therapy. The machine used was of the mechanical rectifier type, furnishing up to 30 ma. at 200 kv. A target-chamber distance of 80 cm. was used throughout the experiments. In Figure 2 are given the absorption curves for this radiation in air, on the surface of the phantom, and at a depth of 10 cm. in the paraffin. The field irradiated in this case was about 1000 sq. cm. Curve 1 shows the absorption of the radiation of the beam

Fig. 1. Paraffin phantom, ionization chamber, and copper shell filters.

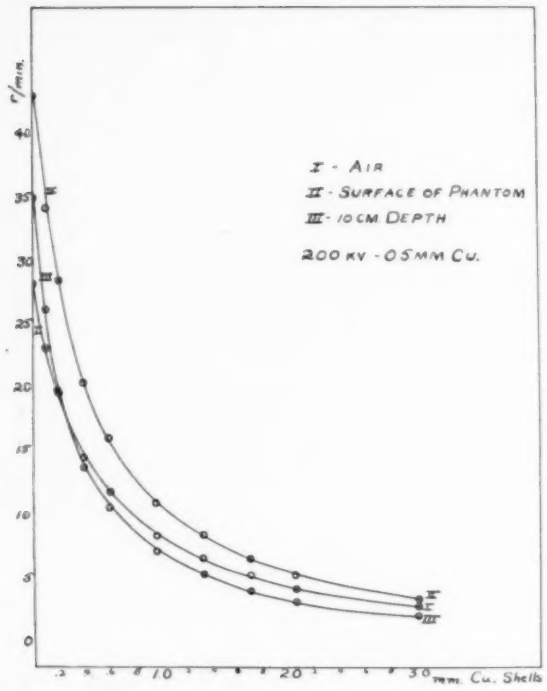

Fig. 2. Curves showing variations in quantity of radiation transmitted by copper shell filters in air, on surface of phantom, and at 10 cm. depth.

in air (before it reaches the patient, when radiation therapy is under consideration). Curve II refers to the radiation effective at the surface of the phantom (skin of the patient), and Curve III to that at a depth of approximately 10 cm. It is evident that the amount of radiation reaching the chamber is very greatly increased by the presence of the scattering body—from 28 to 43 roentgens per minute for this particular beam. That is, the portion of the direct beam reaching the chamber in air delivers there 28 r per minute. But as soon as the scattering substance is placed behind it, radiation scattered to the chamber from other parts of the beam brings the total up to 43 r per minute. Even at a depth of 10 cm. in paraffin there are still 35 r per minute at the chamber, which means that the scattering at this depth more than compensates for the absorption of the primary beam in the medium. *This does not represent a depth dose. No depth doses are given in this paper.* The ionization chamber was kept at a constant distance from the target, so that the change in quantity due to the presence of the scattering medium would not be masked by another change due to change in distance. Since change in distance is one of the important factors in determining depth doses, it follows that no such doses can be derived from the data here presented.

It is evident on examining these curves that the one for radiation at the 10 cm. depth shows much more rapid decrease in the amount transmitted by successive filters than the one for the beam in air—indicating softer radiation. The one for surface radiation shows a quality softer than that in air, but harder than that at the 10 cm. depth. An actual measurement of the amount of change in quality can be obtained from these curves by finding the half-value layers in copper for the three beams, that is, the thickness of copper which reduces the roentgens per minute to half the initial values. They are, for I (air) 0.45 mm.; for II (surface) 0.36 mm., and for III (depth) 0.26 mm. This indicates that

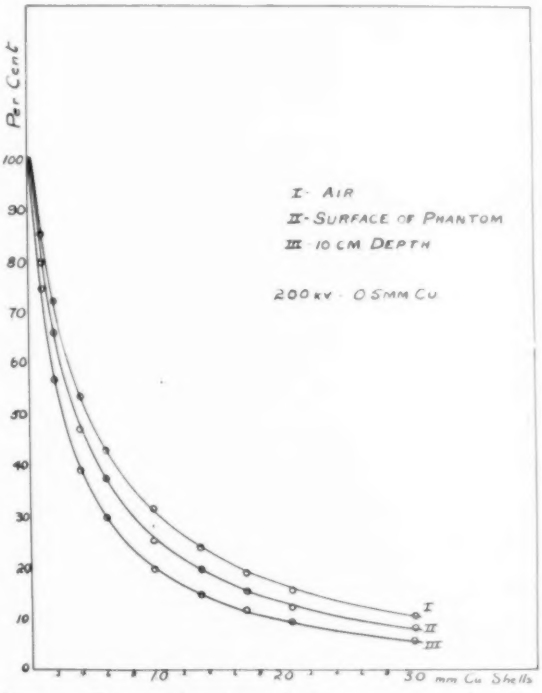

Fig. 3. Curves showing relative amounts of radiation transmitted by successive copper shell filters in air, on surface of phantom, and at 10 cm. depth.

the softening effect is quite marked, and increases considerably with depth in the medium.

The comparison may be more strikingly brought out in another way. If the r per minute with no copper shell around the ionization chamber is taken as 100 per cent for each curve, and the other values in each case calculated on this basis, the curves assume the form shown in Figure 3. Here the change in quality from one to another is apparent at a glance. The half-value layers may be read at the 50 per cent line. As another measure, the effective wave length as determined by absorption in 0.25 mm. copper may be found. It is, for I, 0.222 Å; for II, 0.237Å, and for III, 0.258Å.*

A more graphic comparison may be made in the following manner: In Figure 4 are

* These values are somewhat different from those usually given in the literature. The values depend to some extent on the method used to determine them. In any case, the actual magnitudes are of no importance in the present investigation, because we are interested only in relative magnitudes, and not in absolute values. Since the same method is used throughout the investigation, the type of comparison made is valid.

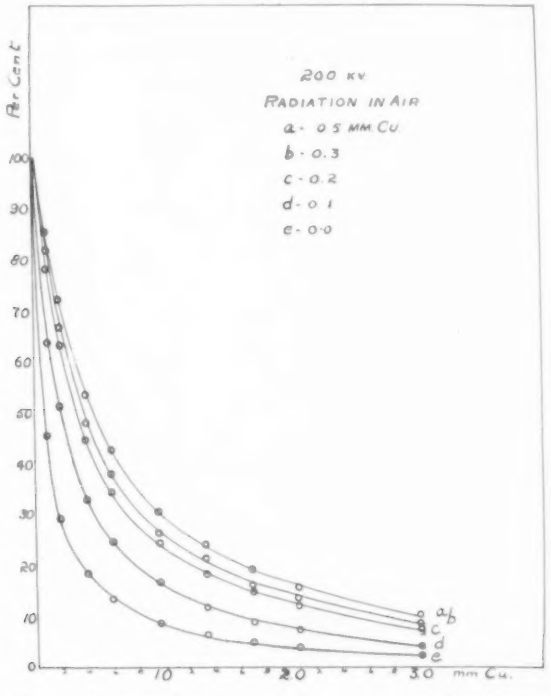

Fig. 4. Curves showing relative amounts of radiation transmitted by successive copper shell filters in air, with varying initial copper filters in tube holder.

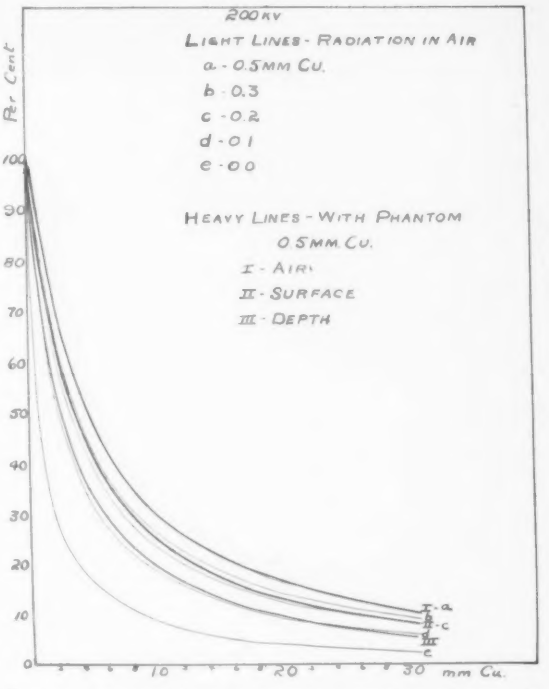

Fig. 5. Comparison of curves showing change in quality of radiation with depth in phantom, and those showing change in quality with change in initial copper filter.

given a number of curves of the type of 1 in Figure 3, for different primary filters. That is, they represent the absorption curves, as determined by the copper shells, for radiation at 200 kv. with successive initial filters of copper from 0 to 0.5 mm. The 0.5 mm. curve is identical with 1 of Figure 3. (The different initial filters must not be confused with the shells. The former are flat filters placed in the diaphragm of the roentgen tube holder. They determine the quality of the beam in air.) The curves of Figure 4 thus refer to a series of radiations which become progressively softer, due to less and less initial filter. Those of Figure 3, as has already been stated, refer to a series which become progressively softer due to the admixture of a larger proportion of scattered radiation. If now, these two sets are superimposed, the amount of softening due to scattering can be expressed in terms of the amount due to change in filter. That is, it is possible to find the type of radiation in air which corresponds in quality ap-

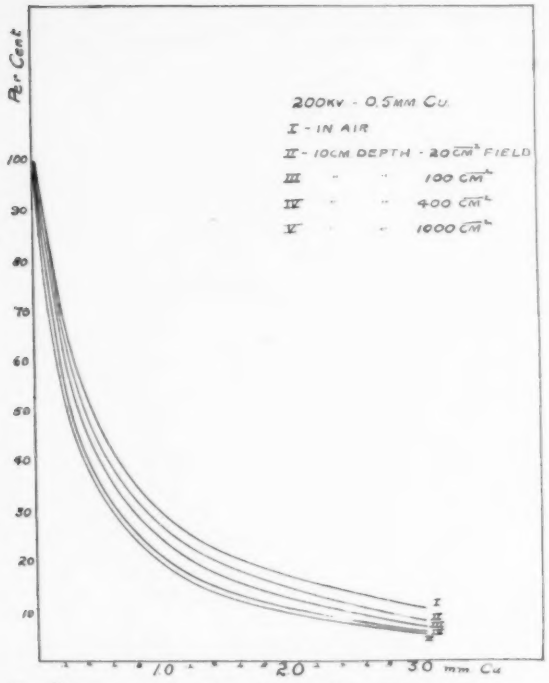

Fig. 6. Curves showing effect of irradiated volume on change in quality at a depth of 10 cm. in paraffin phantom.

proximately to the beam in the depth of the phantom. This is done in Figure 5. The heavy lines refer to the tests with the phantom—the data of Figure 3; the light ones to those in air—the data of Figure 4. Since the first curves in the two sets are identical, they must coincide. II of Figure 3, for surface radiation, is seen to fall quite closely on *c* of Figure 4, representing 0.2 mm. copper initial filter. III of Figure 3, for radiation at 10 cm. depth, corresponds to *d* of Figure 4, for 0.1 mm. copper initial filter. That is, on reaching a depth of 10 cm. in paraffin, radiation which was generated at 200 kv., with an initial filter of 0.5 mm. copper, has been so changed in quality as to be almost identical with a beam in air at 200 kv., with an initial filter of 0.1 mm. copper.

As has been stated, these measurements were made with an irradiated field of 1000 sq. cm. at a depth of 10 cm. in paraffin. It would be expected that the size of the field would influence the result, since the greater the amount of scattering, the greater the change in quality, and evidently a greater volume of irradiated substance provides greater scattering. Accordingly similar measurements were made with different fields—20, 100, and 400 sq. cm., in addition to the data already obtained for 1000 sq. cm. The results are shown in Figure 6. Curve I is the same as Curve I in previous figures, that is, it represents the radiation in air. The others refer to radiation at 10 cm. depth with the different diaphragms, V being the same as III in Figure 3. It is evident that as the diaphragm size decreases, the change in quality also becomes less, and that, particularly at a depth, this effect of the size of the diaphragm is marked. However it should be remembered that the *amount* of radiation reaching a depth through a small field is very much less than that through larger ones—for the extreme cases here given, the quantity is three times as much for the largest field as for the smallest. That is, with a large field, we have a large amount of relatively soft radiation, while with a smaller one we have a considerably smaller amount of relatively harder radiation. We have little indication at present as to which is clinically more desirable. However it may be possible that in some cases this increased hardness of radiation with a small field may compensate for a decrease in quantity from that which would have been delivered with a larger one.

Since the 100 sq. cm. field is commonly used in therapy, certain other types of radiation were tested for this particular field. These were: with 200 kv. (1) 2.0 mm. copper initial filter, which is increasingly more widely used; (2) 0.5 mm. silver, which in some clinics is preferred to the thicker copper filter, and (3) with 165 kv., 0.5 mm. copper. Data for these radiations are given in Table 1.

Since there is some discussion among radiologists as to the choice between 2 mm. of copper and 0.5 mm. of silver, it is of interest to examine these data in detail. This may be done with the aid of Figure 7. The curves are those for the 2.0 mm. copper

filter, plotted in the same manner as those of Figure 3. The points enclosed in the circles are the values for the 0.5 mm. silver initial filter. These curves show, as do the data of the table, that the radiation transmitted by the silver filter is a little the harder of the two, both at the surface and in the depth. Whether this difference in quality is significant in therapy it is impossible to state at the present time. However, it is of interest to note that the difference in quality is measured by the difference in quantity of radiation transmitted by successive shells, and in this case, the advantage, although slight, is definitely with the silver. In other words, although the initial intensities with these two filters are the same, the intensities after traversing a certain amount of subsequent filter, show differences, those with the silver initial filter being always higher.

Incidentally this type of comparison of the two beams of radiation shows the lack of accuracy arising from the use of only the effective length—or of any other method depending on the absorption of the radiation in thin layers of filter—for by such methods the beams transmitted by 2.0 mm. copper and 0.5 mm. silver can be shown to be identical, while our analysis shows a definite difference.

Having shown that, by this method of investigation, marked changes in quality of radiation are found after its passage through tissue, it is important to investigate the accuracy of the method, or the possible errors inherent in it. These possibilities are of two sorts, those arising from the use of paraffin instead of tissue, and those inherent in the ionization chamber itself. The first were investigated experimentally. Twenty pounds of fresh meat were obtained in large pieces, which were

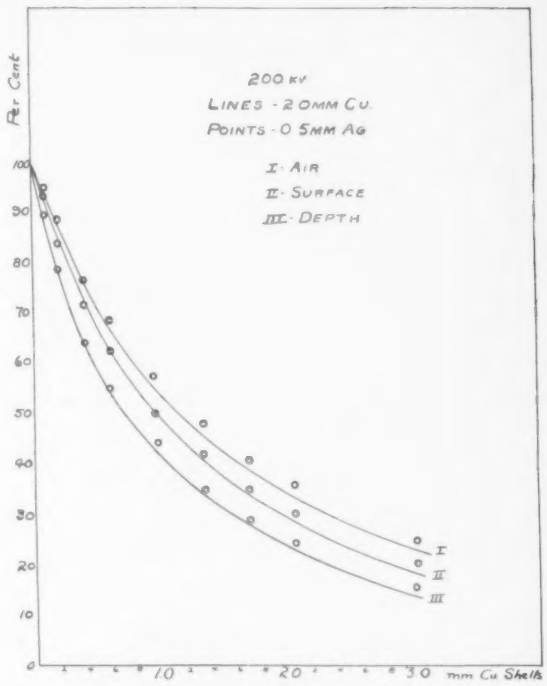

Fig. 7. Curves showing difference in change of quality with depth, for initial filters of 0.5 mm. silver and 2.0 mm. copper.

Table I

Change in Quality of Various Beams of Roentgen Rays on Passing Through Paraffin

kv.	Initial Filter	Quality					
		Air		Surface		10 cm. Depth	
	mm.	Eff. Wave Length	Half-Value Layer in Cu	Eff. Wave Length	Half-Value Layer in Cu	Eff. Wave Length	Half-Value Layer in Cu
		Å	mm.	Å	mm.	Å	mm.
200	0.5 Cu	0.206	0.46	0.218	0.41	0.236	0.36
200	2.0 Cu	0.152	1.14	0.175	0.90	0.198	0.70
200	0.5 Ag	0.154	1.23	0.173	0.95	0.192	0.73
165	0.5 Cu	0.220	0.43	0.283	0.39	0.250	0.30

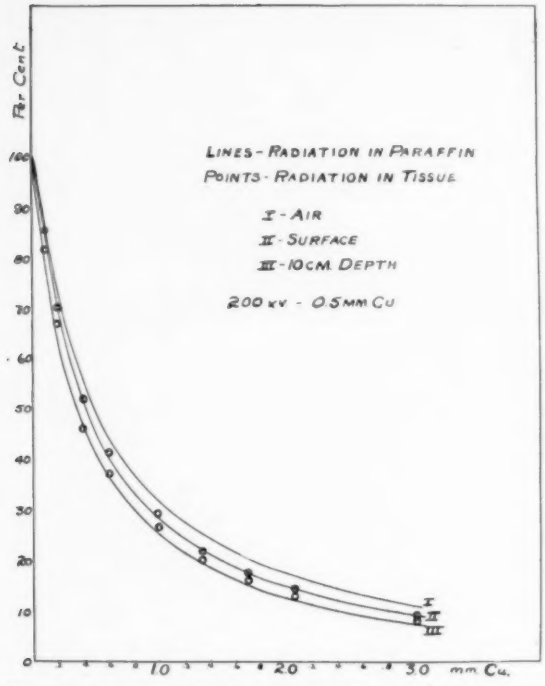

FIG. 8. Curves showing comparison of change of quality with depth as measured in paraffin and in tissue.

cut and tied together in masses similar in size and shape to the pile of discs of paraffin. A depression was made in one to receive the chamber, and the thickness of tissue used above it, for the study of the depth radiation, was as nearly as possible the same as that of the paraffin. Comparisons were made for two voltages, 200 and 165 kv., 2 filters 0.5 and 2.0 mm. of copper and 2 fields, 100 and 400 sq. cm. The data for 200 kv., 0.5 mm. Cu, and 100 sq. cm., are given in Figure 8. The lines are drawn through the data for the paraffin, the points represent the values for the tissue. For the surface radiations, the quality of the beams in tissue and paraffin are the same, within the limits of experimental error. For the radiation at a depth of 10 cm., that in the meat seems to be a little harder than in the paraffin. It is difficult to state whether this is an actual variation or is due to a difference in the thickness of the scattering substance. It was difficult to determine the exact thickness of the meat, and also to keep it absolutely constant. However, the maximum difference between the two curves, with the thickest filter, is small. Such variations are not serious at present, but they indicate that if accurate data are desired they must be taken into account. For the other beams investigated the variations were of the same order. Evidently the radiation behaves in the two media in nearly enough the same manner so that no serious error will be introduced in using paraffin as a first approximation to conditions in tissue.

With regard to errors introduced by the shape, size, and material of the chamber itself, it may be stated at once that the chamber is too large to permit the obtaining of accurate values of the actual amount of energy reaching a very small volume in the tissue. It was thought advisable to have a large chamber, in order to have fairly large ionization currents. This work must, from this point of view, be regarded as preliminary. It is hoped to repeat it with a much smaller chamber, since such large differences in intensity exist. This effect of the size of the chamber does not appreciably affect the accuracy of the comparison of the qualities of the radiations, since the same chamber was used throughout, and comparisons are made for the same given regions. What it does prevent is the use of values such as those of Figure 2 as measurements of actual amounts of radiation delivered at any specified point.

However the important problem with regard to the chamber is whether it possesses any property which makes its readings vary with the quality of the radiation affecting it, in such a manner as to introduce an extraneous effect. This can be determined by direct comparison with a standard open air ionization chamber. Such a comparison was made in the following manner: The air chamber was mounted under the roentgen tube at the distance regularly used for the ping-pong chamber in the experiments. Limiting diaphragms were interposed between it and the tube, to eliminate stem radiation. Copper absorption curves were made at 200 and 165

kv., the filters being flat sheets of copper. The standard chamber was then removed, the intermediate diaphragm being left in place, the ping-pong chamber set up in the same place, and two more sets of absorption curves made, the filters being first the same flat ones as were used with the standard chamber, and second the shells used in the usual manner. The results are shown in Table II, giving the ratio between the values of the output of the roentgen tube in roentgens per minute as measured by the two chambers for both sets of filters. These values were obtained in the usual manner for each chamber by the use of a measuring instrument calibrated to read in electrostatic units per second. This value, multiplied by 60 and divided by the volume of the ionized air, gives the number of roentgens per minute.

TABLE II

COMPARISON OF PING-PONG AND STANDARD AIR IONIZATION CHAMBERS

Filter mm. Cu	200 kv.					165 kv.				
	r/min.			Ratio Air/Ping-Pong		r/min.			Ratio Air/Ping-Pong	
	Air	Ping-Pong		Flat Filters	Shells	Air	Ping-Pong		Flat Filters	Shells
		Flat Filters	Shells				Flat Filters	Shells		
0	82.5	81.0	81.0	1.02	1.02	55.0	55.3	55.3	1.00	1.00
0.1	52.5	55.5	51.8	0.95	1.01	34.5	34.8	34.2	0.99	0.99
0.2	40.2	43.3	38.0	0.93	1.06	24.0	27.0	23.2	0.89	1.03
0.3	32.5	36.2	29.8	0.90	1.09	19.3	22.1	18.0	0.96	1.07
0.4	27.5	28.1	26.1	0.98	1.06	15.8	18.5	13.9	0.86	1.14
0.5	24.6	27.4	22.5	0.90	1.09	13.7	16.2	12.3	0.85	1.11
0.6	21.8	24.4	19.8	0.90	1.10	11.8	14.0	10.3	0.85	1.14
0.8	17.7	19.8	16.0	0.90	1.10	9.0	10.6	8.1	0.85	1.12
1.0	15.0	16.4	13.5	0.92	1.11	7.2	8.5	6.5	0.85	1.11
1.5	10.5	10.7	9.0	0.98	1.17	4.3	5.1	4.0	0.85	1.08
2.0	7.5	7.7	6.3	0.98	1.19	2.9	3.3	2.5	0.88	1.16
2.5	5.8	5.9	4.9	0.98	1.18	2.0	2.3	1.65	0.87	1.21
3.0	4.7	5.0	3.9	0.96	1.20	1.7	1.7	1.4	1.00	1.20

The comparison of the two chambers with the flat filters shows that the ping-pong chamber has a wall effect which makes it read from 5 to 15 per cent higher than the air chamber, for radiation of the qualities in which we are interested. However, with the shells, the ping-pong chamber reads consistently lower than the air chamber. This is to be expected, since, due to the curvature of the shells, part of the rays reaching the chamber will have traversed a greater thickness of copper than that indicated, thus lessening the amount of radiation producing ionization within the chamber. This will be partly compensated for by the scattering into the chamber by the further half of the copper shell, but apparently, in air, the loss is not completely balanced. When the whole chamber is surrounded by a scattering medium, so that rays enter it from all directions instead of in a limited beam, the situation will be somewhat different from either of these, and the result will probably be intermediate between the other two and lie closer to the air chamber values than either of them. It is evident that there are no anomalous effects which might affect the *relative* positions of the curves, which is all that matters in the present investigation.

It is hoped in the near future to repeat this work with a smaller ionization chamber, and an arrangement which will more closely parallel values given by the standard chamber, and to extend the observations to much more penetrating roentgen and gamma rays.

As far as the practical applications of these data are concerned, at present there is little to say. Before any conclusions can be reached regarding the most desirable quality of radiation for various purposes, it will be necessary to have a great deal more biological data. But as information of this sort becomes available, the method here described gives a means for determining the quality of the radiation which has actually been found most effective in a given case. It will also make it possible to reproduce a particular quality under somewhat different physical and clinical conditions.

CONCLUSIONS

1. A method has been developed for determining the quality of roentgen rays (or gamma rays) at a point within a mass of material.

2. By this means, the change in quality of a beam of radiation during its passage through a scattering substance can be investigated.

3. Such investigations have been made for several different beams of roentgen radiation. A considerable change in quality has been found in every case.

4. This change in quality, consisting of a softening of the radiation, increases with an increase of depth in the scattering material, and also with an increase in the size of the irradiated area.

5. An analysis of beams of radiation by this method is shown to be more satisfactory for purposes of comparison than the use of the effective wave length of the half-value layer. Certain beams which were identical when tested by the latter standards were shown to vary appreciably by the former.

6. The method offers a possible means of comparing effects to be expected in the tissues from different beams of radiation, and of determining the optimum quality to produce a given effect.

The authors wish to acknowledge their indebtedness to Dr. Failla, who originated the method, and whose interest and advice have been of value throughout the course of the work.

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CONCERNING THE VISIBILITY OF ROENTGEN RAYS*

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IT IS so generally accepted that roentgen rays are not visible to the naked eye, that few, if any, workers have taken the trouble to verify the statement for their own satisfaction. Regardless of the well-founded belief to the contrary, the rays are visible to the unaided human eye.

Some time ago, while working with a crystal spectroscope in a darkened room with eyes well accommodated, I happened to let the unobstructed beam strike me in the face. The effect was so startling that I remarked to my assistant that my eyes were fluorescing. He laughed at the statement and remarked that such a thing was impossible. Recently while using a roentgenoscope, a similar experience occurred. Believing that it was not simply a matter of imagination, I decided to risk some exposure. With well-accommodated eyes, I faced the tube in a standard make roentgenoscope. At a voltage of 95 kv. and 5 ma., with a distance of about 20 inches, the tube was energized. The sight of the rays was very apparent. The sensation was that of looking into a blue-gray mist. Of course, the point of emanation could not be made out, but by moving the head around, the portal was accurately outlined. Closing the eyelids made no difference. An increase or decrease of the milliamperage was plainly distinguishable. At first it seemed reasonable that as the rays were not obstructed by the iris, accommodation to light would not be of any significance. Accordingly, I went out into the sunlight, allowing my pupils to contract, and on returning to the machine found that the rays were no longer visible. Then, however, I realized that the light accommodation is more than a function of the iris and that the "visual purple" of the retina has to be built up slowly before the eye is sensitive.

Having exposed myself all that seemed wise for one who is practising roentgenology, I called in a medical student, telling him nothing except that I wanted him to look in the direction of the tube and describe what he saw. The tube was energized but the shutter was closed. As soon as the shutter was opened (with no sound that could give a clue to the observer) he stated that a blue-gray light had been turned on but that he could not determine its point of origin. Attempts to deceive him by asking him if it was visible showed that he could readily tell when the shutter was opened or closed.

Following this, I called in a physician well skilled in eye diseases, who described the phenomenon similarly.

The impression which the observer gets is that there is some part of his eye which is fluorescing, despite the fact that the light stops as soon as the ray is stopped with no afterglow. Therefore, I attempted to see the glow in the eyes of another individual. As this experiment met with failure, a dog was exposed to a powerful ray and its eyes examined for fluorescence. Dead beef eyes were cut open and observed under a powerful ray also but in none was any glow seen.

As all of these experiments had been conducted on the same instrument, namely, a bakelite top roentgenoscopic table, I felt it well to rule out the possibility of some source of error by making tests on other pieces of apparatus. Therefore as shown in Figure 1, the following types of apparatus were used: A Müller Metalix tube, a CDX dental unit and the Model A Shockproof Unit. The last two being completely shielded in grounded metal containers certainly ruled out the possibility of any electrical phenomenon.

A number of individuals have been tested, including negroes, and all describe the appearance similarly.

* Read at the Thirty-second Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 22–25, 1931.

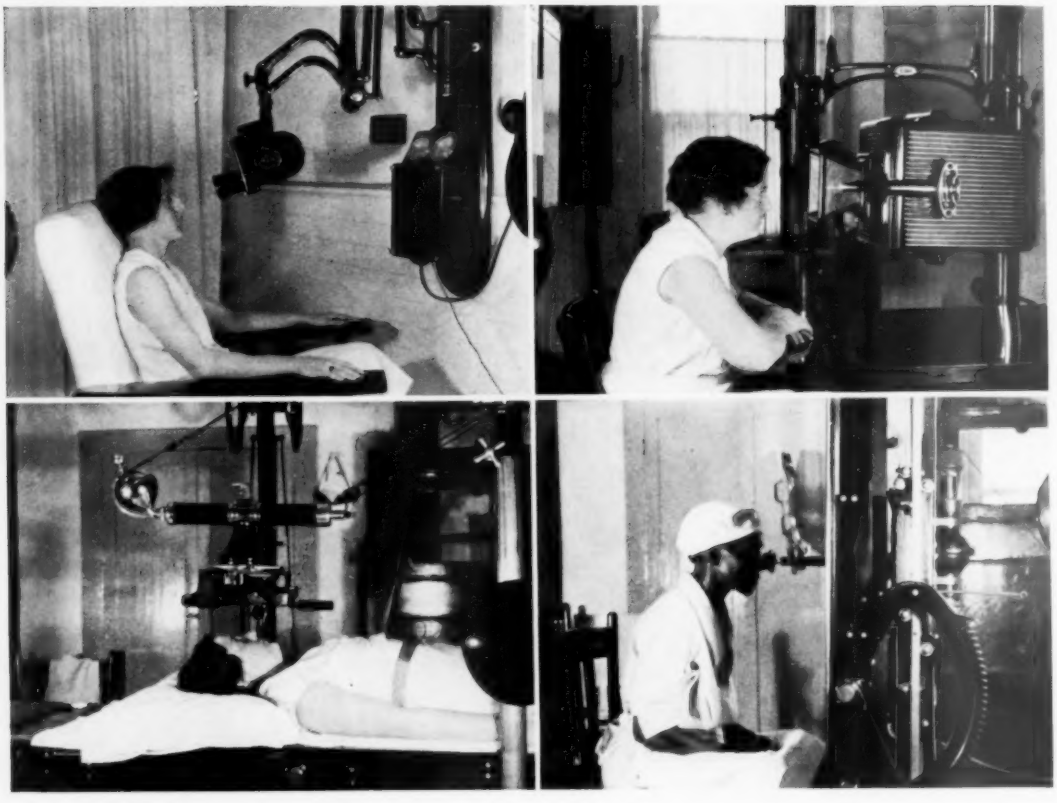

Fig. 1.

Believing that if any reference could be found to experiments of this kind, it would most likely be in the old writings, I studied a number of old textbooks. The only mention was in Kassabian[1] as follows: "Prof. E. Dorn asserts most positively that the X-rays are *visible*, opinions to the contrary notwithstanding."

As the information in Kassabian was not very clearly given, I obtained the original work[2] from which it was taken and quote the following:

With the co-operation of Dr. Dittenberger, I have made a series of researches upon the possibility of a stimulation of the nerves by electrical actions taking place in the neighborhood of the head. A cardboard cylinder was placed over the head, and rendered light-tight by means of velvet. Under these circumstances it was definitely ascertained that the observer saw the Roentgen Rays distinctly. An aluminium sheet, 1.03 millimetres thick, 60 centimetres long, and 45 centimetres broad, somewhat weakened the appearence when interposed, but did not produce extinction of the phenomenon. Then I allowed the sparks (10 centimetres long) of the induction coil, which had supplied the tube, to jump across the space previously occupied by the tube, at a distance of about 10 centimetres from the eye; *there was not, however, the faintest sensation of light.* Equally little was this the case when using a Himstedt's apparatus for Tesla currents, although I experimented with spark-lengths of 4, 6, 10, and 16 centimetres, and with horizontal and vertical positions for the spark-path.

Corresponding observations were made with another arrangement of head-covering—namely, black paper over the eyes, and velvet over the head—with similar negative results, in spite of the fact that in this case the length of the Tesla sparks was increased in 21 centimetres, and the observer was situated with the region of his eyes in the glow of the discharge.

The most striking refutation of the suggestion that the sensation of light excited by Roentgen tubes is an illusion due to electrical

influences is, however, afforded by the following experiment:

The Roentgen tube was turned backwards, that is to say, with the back of the anti-cathode presented towards the eye. The eye, accustomed to darkness, could not detect the smallest action, although the appearance of light was distinctly seen, both before and afterwards, with the tube in the right position. The tube thus reversed in position produced only a very faint fluorescence upon a barium-plantinocyanide screen.

Meantime, Herr Roentgen has himself confirmed the visibility of the rays discovered by him, and has given an elegant modification of the fundamental experiment. If an absorbing metal plate with a narrow slit in it is held before the eye, there is perceived a bright line, which is either straight or curved according to the relative positions of the anti-cathode, slit, and eye.

Before I had received information of this, I made a similar observation in which I saw the 'Roentgen shadow' of a straight brass rod 5 millimetres thick appearing under certain conditions as a curved shadow upon the retina.

The result of both experiments is easily explained. To me my experiment was important, because I perceived the curvature by observation without any previous deliberation, and the unexpected result offered, therefore, a welcome confirmation for the view that I was not dealing with an illusion due to subjective phenomena of light.

Another reference by two French writers[3] was found giving their reasons why the roentgen rays were *not* visible to the eye. Their conclusions were that the roentgen rays were not able to pass through the vitreous and aqueous humors and therefore could not reach the retina. There followed a series of experiments in which pig eyes were placed on plates and exposures made of half hour duration. No penetration through the eyes was accomplished. Of course the futility of their experiments lay in the fact that they were using a very low power tube and static machine which did not have sufficient penetration to drive the rays through the thickness of a pig's eye.

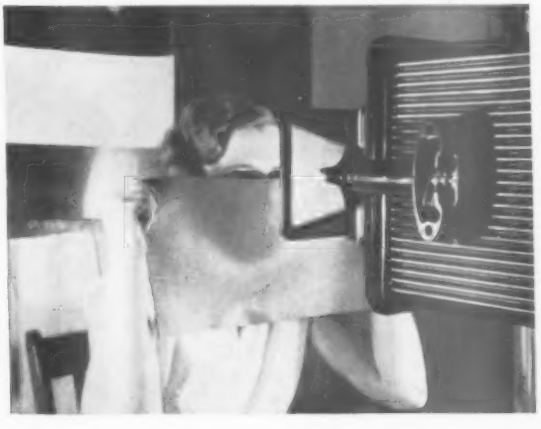

Fig. 2.

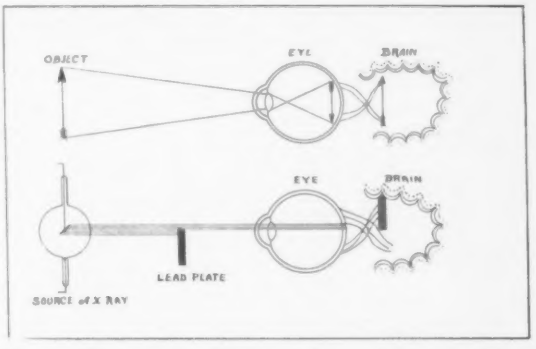

Fig. 3. The upper diagram shows how an object, when seen in ordinary light, makes an inverted image on the retina, which is again inverted to its correct position in the brain.

The lower diagram shows a lead plate intercepting the roentgen rays to prevent their striking the lower part of the retina. As the image is inverted in the brain, the plate appears to the observer to cover the upper part of the eye. Both of these diagrams are rather free.

Thomas Edison was quite familiar with the visibility of the roentgen rays and the *Electrical Engineer* of 1896 describes some experiments of his on a child who was totally blind to ordinary light but who was quite able to see the roentgen rays.[4]

Perhaps the most striking experiment along this line is one which I found accidentally and have never seen mentioned elsewhere. If a plate of lead or other opaque material is raised up along the face of the observer, as shown in Figure 2, it will seem to him to be lowered from the top of the face. The explanation of this is that visible light is inverted by the refractile parts of the eye so that the image in reality is upside down on the retina, the brain again placing it in its normal position in the

visual area. Roentgen rays, on striking the eye, are not refracted by any of the parts and therefore when the lower part of the retina is shaded, the brain sees the upper shaded. This experiment, to my mind, clears up any possible remaining doubt that the roentgen rays are really seen and rules out all chance of experimental error. This is shown on the rather free diagrams in Figure 3.

In conclusion, there seems to be no practical application of these investigations but it is interesting to find how few modern roentgenologists are familiar with them while they were well known to the investigators of 1896.

The roentgen rays may be visible by their direct action on the retina, or it is possible that some part of the eye gives off visible light by fluorescence. However, I have never been able to detect that fluorescence on the eyes of another individual or in any parts of dissected eyes.

I am in indebted to Dr. Otto Glasser for several of the references.

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2. Dorn, E. On the visibility of the roentgen rays. *Arch. Roentg. Ray, Lond.*, 1898, *2*, 69–70.
3. Dariex and de Rochas. Sur la cause de l'invisibilite des rayons de Röntgen. *Compt. rend. Acad. d. sc.*, 1896, *122*, 458.
4. Clark, G. W. Electrical Engineer, Dec. 9, 1896, 601.

DISCUSSION

Dr. G. Failla, New York City. In regard to Dr. Taft's paper, I should like to add that gamma rays also produce the effect which he has described. If a radium tube is brought close to the eyes in a dark room, one notices a greenish glow, accompanied, in my eye, at least, by a peculiar sensation. I believe I have seen this described in the literature, but I cannot give the reference. The effect has been attributed to fluorescence, either in the retina or the lens.

Dr. A. U. Desjardins, Rochester, Minn. I happen to be familiar with some of the early work and some of the early publications on this subject, because I have been reviewing all previous experimental and clinical work on the effects of roentgen rays and radium on the eye. For a short time Roentgen himself thought the rays were visible, but later he changed his mind and made the statement that the rays were not visible. A short time later, I think about 1903, London, of St. Petersburg, working with radium first, observed this green light, and being an ophthalmologist, he got the notion that perhaps this could be used to teach blind people to read. Later still he claimed that results could be obtained in this way, but the nature of such results were not specified. The substance of a paper read by him at a meeting in Vienna was published in one of the Vienna newspapers; this made such an impression that the Emperor of Germany commissioned Graefe to study the question and report. Graefe spent several months going into the entire matter and finally reported that neither the gamma rays nor the roentgen rays are visible, but that the impression of light in the eye was due to fluorescence of the retina. From that time until Dr. Taft just now surprised us, it has been assumed that the rays are invisible.

Dr. Taft (closing). Concerning Dr. Failla's question about radium, I have not tried it as I have not enough radium. It is improbable that a small quantity would be sufficient.

Dr. Failla. I have seen it with as little as 10 mg.

Dr. Taft. Thank you, I am glad to hear you say that. I have stated in my paper that I cannot determine whether the visibility is due to fluorescence in the eye or to actual stimulation of the retina. I do not believe that the matter can be definitely settled. To those of you who doubt that the roentgen rays have any visibility at all, I suggest that you accommodate your eyes properly, get directly in the beam, and I assure you that you will see something.

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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

Editor: Lawrence Reynolds, M.D.

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Thirty-third Annual Meeting: Detroit, Mich., Sept. 27–30, 1932.

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Eighteenth Annual Meeting: To be announced.

Committee on Arrangements: E. C. Samuels, Chairman, 3503 Prytaria St., New Orleans, La., E. R. Bowie, L. J. Menville, L. J. Williams.

EDITORIAL

ASBESTOSIS

THE economic importance of asbestos and its by-products has been recently emphasized at the Imperial Economic Conference held in Ottawa. This importance is shown by its being one of the principal topics for discussion and for adjustment of tariff laws between the Dominions and the Mother Country. The widespread employment of asbestos in its many commercial, industrial and household uses make it also of importance from a medical standpoint because it has been observed for a long time that workers in asbestos factories who are constantly exposed to the dust are subject to pulmonary disturbances. One of the earliest case reports was given by Murray[1] in 1900. His report was of a man who worked in a factory for ten years, mostly as a carder, and was the sole surviver before his death of ten other men who started work with him. The autopsy in this case revealed pulmonary fibrosis. Photomicrographs of sections of the lungs showed large spicules of asbestos, at least they were so regarded at that time. The second report was apparently by Fahr,[2] in 1914, who demonstrated to the Medical Society of Hamburg specimens and photomicrographs of the lungs from a case of pneumoconiosis occurring in an asbestos worker. He mentioned the presence in the lung of a large number of crystals and stated that similar structures had been seen in 1906 by Marchand and Riesel[3] who had speculated as to whether they were due to the inhalation of asbestos dust or were a hemoglobin derivative.

Since then numerous references and case reports have been given in the literature, especially by Cooke,[4] Oliver,[5] McDonald,[6] Pancoast and Pendergrass[7] and others.

That pneumoconiosis following inhalation of asbestos dust is not an infrequent occurrence is shown by the recent references in the literature, notably by Lynch and Smith,[8] who in a survey of all the available literature on the subject up to the time of their paper, collected 172 cases of pulmonary asbestosis. The majority of these cases have been reported from the British Isles though isolated reports have been given from South Africa and more recently from Germany.[9] The Report of the Chief Inspector of Factories and Workshops for 1931[10] records the death in England of 9 cases. It is of interest to note in this report that the average length of employment in the fatal cases of silicosis is more than twice as long as in the fatal cases of asbestosis.

Asbestos is a peculiar fibrous and crystalline mineral composed almost entirely of silicates, mainly of hydrate magnesium silicate, with varying admixtures of those of aluminum and iron. The minerals differ in their exact constituency, especially as to the amount of iron and aluminum, in different countries in which they are found and mined. Asbestos is definitely but mildly irritating to the body tissues. It is believed by some that the pulmonary changes seen

[1] Murray, M. *Charing Cross Hosp. Gaz.*, 1900. Quoted by Pancoast and Pendergrass.

[2] Fahr. Quoted by Gloyne, S. R. The asbestosis body. *Lancet*, June 25, 1932, *1*, 1351–1355.

[3] Marchand and Riesel. Quoted by Gloyne.

[4] Cooke, W. E. Quoted by Pancoast and Pendergrass.

[5] Oliver, T. Quoted by Pancoast and Pendergrass.

[6] McDonald, S. Quoted by Pancoast and Pendergrass.

[7] Pancoast, H. K., and Pendergrass, E. P. Review of pneumoconiosis. Am. J. Roentgenol. & Rad. Therapy, 1931, *26*, 556–614.

[8] Lynch, K. M., and Smith, W. A. Pulmonary asbestosis. *Am. Rev. Tuberc.*, 1931, *23*, 643–659.

[9] German work on pulmonary asbestosis. *Lancet*, July 9, 1932, *2*, 92–93.

[10] Report of the Chief Inspector of Factories and Workshops for 1931. H. M. Stationery Office, 1932, pp. 155.

in asbestosis are due to the presence of silica. However the constant finding of so-called asbestosis bodies in the autopsy material and in sputum tends to refute this impression. These so-called "curious bodies" or asbestosis bodies vary in length as well as in size and shape. Apparently they are composed of a central core which is probably an asbestos spicule upon which colloidal aggregates of blood protein have been adsorbed. Whether or not these asbestosis bodies will ultimately prove to be the causative factor in the fibrosis remains to be proved but the fact is that they are universally present in all cases of asbestosis. Beintker[11] and Timmermans[12] believe that the asbestosis bodies arise through the deposition, due to the solution of the asbestos, of a colloidal form of liberated silicic acid on the central core of the asbestos fiber. They believe that in asbestosis the silicic acid acts as a chemical irritant which leads to fibrosis and that this extreme fibrosis leads to such marked discrepancy between the clinical appearances and symptoms on the one hand and the roentgen picture on the other. Even the most severe cases of asbestosis did not give as pronounced a roentgen picture as that of silicosis and they feel that the discrepancy between the clinical picture and the roentgen findings is a characteristic peculiar to asbestosis.

Asbestosis is of particular interest to roentgenologists because of the lung changes. These changes are usually manifest in three stages: first, an increase in the normal lung striation with the appearance of a fine, not very clearly defined network; second, a thicker network with delicate, sharply defined opaque spots, and third, an intensification of this network to form a shadowy veil covering the lung. The signs are first seen and are most marked in the mid-zone and lower lobe areas; the contour of the heart shadow becomes ill defined in the second stage. Pancoast and Pendergrass[7] have called attention to the necessity of the finest type of roentgenograms for the portrayal of these changes and they also call attention to the importance of a roentgenoscopic study of the diaphragmatic movements as apparently the actual state of disability present as shown by the restriction in the movements of the diaphragm is out of all proportion to what one would expect from a study of the roentgenogram.

Whether or not asbestosis predisposes to tuberculosis is not determined. In the early cases pulmonary tuberculosis was reported as an accompanying condition in a few instances. Merewether and Price[13] stated that asbestosis differs from silicosis in the distribution of the fibrous tissue, a more rapid development, in roentgenographic features and possibly in a lessened susceptibility to tuberculosis. Merewether states that out of 374 cases examined evidence of active tuberculosis was found in three and he is under the impression that while there is no outstanding susceptibility proved he does not agree that the question has been finally settled.

While it is to be expected that the majority of cases of asbestosis will undoubtedly occur in districts where the factories are located, with the shifting population from one industrial center to another which is so prevalent at the present time, the importance of asbestos as an etiological factor in the production of pneumoconiosis should not be overlooked.

[11,12] *Lancet*, July 9, 1932, *2*, 92–93.

[13] Quoted by Pancoast and Pendergrass.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. E. P. Pendergrass, University Hospital, Philadelphia, Pa.
Annual Meeting: Detroit, Mich., Sept. 27–30, 1932.

American College of Radiology
Secretary, Dr. Albert Soiland, 1407 S. Hope St., Los Angeles, Calif.
Annual Meeting: Milwaukee, Wis., 1933.

Section on Radiology, American Medical Association
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio.
Annual meeting: Milwaukee, Wis., 1933.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y.
Annual Meeting: Atlantic City, N. J., Nov. 28–Dec. 2, 1932.

Radiological Section, Los Angeles County Medical Society
Secretary, Dr. D. R. MacColl, 2826 S. Hope St., Los Angeles, Calif.
Meets on the third Wednesday of each month at the California Hospital.

Radiological Section, Southern Medical Association
Secretary, Dr. C. H. Heacock, 20 S. Dunlap St., Memphis, Tenn.
Annual meeting: Birmingham, Ala., Nov. 16–18, 1932.

Brooklyn Roentgen Ray Society
Secretary, Dr. J. J. Masterson, 401-76th St., Brooklyn, N. Y.
Meets monthly on first Tuesday, October to April.

Buffalo Radiological Society
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y.
Meets second Monday of each month except during summer months, place of meeting selected by the host.

Chicago Roentgen Society
Secretary, Dr. George M. Landau, 660 Groveland Park.
Meeting; second Thursday of each month October to May inclusive at Virginia Hotel.

Cincinnati Radiological Society
Secretary, Dr. H. G. Reineke, Christian R. Holmes Hospital, Cincinnati, Ohio.
Meetings held monthly.

Cleveland Radiological Society
Secretary, Dr. M. A. Thomas, Medical Arts Bldg
Meetings are held at 6:15 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital.
Meets monthly on first Thursday from October to May, at Wayne Country Medical Society Building.

Florida Radiological Society
Secretary, Dr. W. McL. Shaw, 418 St. James Bldg., Jacksonville, Fla.
Meetings held twice a year, May and November.
Next meeting, Jacksonville, November, 1932.

Illinois Radiological Society
Secretary, Dr. L. M. Hilt, Myers Bldg., Springfield, Ill.
Regular meetings held quarterly.

Indiana Roentgen Society
Secretary, Dr. J. N. Collins, Indianapolis, Ind.
Annual meeting each February 22 in Indianapolis.

Milwaukee Roentgen Ray Society
Secretary, Dr. J. E. Habbe, 221 Wisconsin Ave., Milwaukee, Wis.
Meets first Friday in October, December, February and April.
Place of meeting designated by the president.

Minnesota Radiological Society
Secretary, Dr. L. G. Rigler, University Hospital, Minneapolis, Minn.

New England Roentgen Ray Society
Secretary, Dr. Thomas R. Healy, 370 Marlboro St., Boston, Mass.
Meets monthly on third Friday, Boston Medical Library.

New York Roentgen Society
Secretary, Dr. J. Bennett Edwards, Englewood Hospital, Englewood, N. J.
Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

Central New York Roentgen Ray Society
Secretary, Dr. M. T. Powers, 250 Genesee St., Utica, N. Y.
Three meetings a year—January, May and November.

Pennsylvania Radiological Society
Secretary, Dr. W. E. Reiley, Clearfield, Penna.
Next Meeting: Philipsburg, Pa., May 18–19, 1932.

Philadelphia Roentgen Ray Society
Secretary, Dr. Karl Kornblum, 3400 Spruce St.
Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thomson Hall, College of Physicians, 19 S. 22d St.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Camp C. Thomas, 476 Lake Ave.
Meets monthly on the first Friday evening at 7:45 at the Rochester Medical Association Building.

St. Louis Roentgen Club
Secretary, Dr. W. K. Mueller, University Club Bldg.
Meets first week of each month. Time and place of meetings designated by president.

Texas Radiological Society
Secretary-Treasurer, Dr. C. P. Harris, Houston, Texas.
Meets annually one day preceding the meeting of the Texas State Medical Association.

University of Michigan Roentgen Ray Society
Secretary, Dr. C. C. Taylor, University Hospital, Ann Arbor, Mich.
Meets first and third Wednesday evening of the month from October to June, at 8 o'clock in the amphitheatre of the University Hospital.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Virginia Roentgen Ray Club
Secretary, Dr. Wright Clarkson, 205 S. Sycamore St., Petersburg, Va.
Meets annually in October.
Next meeting: Richmond, Va., October, 1932.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 p.m., at 32 Welbeck St., London, W. 1., or as advertised.

Electro-Therapeutic Section of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:30 p.m. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Colin Macdonald, Lister House, 61 Collins St., Melbourne, Australia.
Meets monthly at Melbourne during the winter.

Section on Radiology, Canadian Medical Association
Secretary, Dr. A. H. Rolph, 160 St. George St., Toronto, Ont.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. P. C. Fenwick, The Hospital, Christchurch. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Allies, 134, Louvain, (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Societe de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, 11/52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd-und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Roentgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the Fall.

Societa Italiana Radiologia Medica
Secretary, Professor M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Maracine 30, Bucarest, Rumania.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson.
Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan. Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime.

Society of Medical Radiology of Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Society of Roentgenology
Secretary, Professor Holzknecht, Vienna, IX, General Hospital.
Meets first Tuesday each month, October to July.

Orient

Japan X-ray Association
c/o Orthopedic Surgery, Tokyo Imperial University.
Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike, Kyoto, Japan. Meets bi-monthly on third Sunday.

PRELIMINARY PROGRAM

OF THE

THIRTY-THIRD ANNUAL MEETING

OF THE

AMERICAN ROENTGEN RAY SOCIETY SEPTEMBER 27–30, 1932

BOOK-CADILLAC HOTEL, DETROIT, MICHIGAN

TUESDAY MORNING, STEPEMBER 27, 1932

Call to Order. Leopold Jaches, M.D., New York City.

Installation of in-coming President.

Announcements.

President's Address. Wm. A. Evans, M.D., Detroit.

Symposium on Joint Pathology:

1. Pathology of Joint Conditions. Ralph K. Ghormley, M.D., Rochester, Minn.
2. The Correlation of Pathological and Roentgenological Findings in the Diagnosis of Tuberculosis of Joints. D. B. Phemister, M.D., and C. Howard Hatcher, M.D., Chicago.
3. Roentgen Diagnosis of Bone and Joint Tuberculosis. Maurice M. Pomeranz, M.D., New York City.
4. Osteochondritis. Maxwell Harbin, M.D., Cleveland, Ohio.
5. Roentgenological Findings in Polyarticular Arthritis. Leo. G. Rigler, M.D., Minneapolis, Minn.

TUESDAY AFTERNOON, SEPTEMBER 27, 1932

Symposium on Industrial and Medicolegal Practice:

1. Relation of Trauma to Arthritis. Howard P. Doub., M.D., Detroit.
2. Trauma as an Etiologic Factor in Cardiac and Pulmonary Disease. L. R. Sante, M.D., St. Louis, Mo.
3. Trauma as an Etiologic Factor in Malignancy. F. W. Hartman, M.D., Detroit.
4. Kienböck's Disease and Allied Conditions. Carl L. Gillies, M.D., Cedar Rapids, Iowa.
5. Bone Atrophy. J. Albert Key, M.D., St. Louis, Mo.
6. Anatomic Basis for Disturbed Function in Evaluating Accidental Injuries. Henry H. Kessler, M.D., Newark, N. J.
7. Traumatic Neuroses. L. J. Foster, M.D., Detroit.
8. The Value of Expert Testimony. Samuel H. Rhoads, Lansing, Michigan.

TUESDAY EVENING, SEPTEMBER 27, 1932

The X-ray in Industry and other Non-Medical Fields. George L. Clark, Ph.D. Chicago, Illinois.

Governmental Responsibility in the Practice of Medicine. Senator Royal S. Copeland, Washington, D. C.

WEDNESDAY MORNING, SEPTEMBER 28, 1932

Symposium on Tuberculosis:

The Significance of the Triangular Basal Shadows in Roentgenograms of the Chest. Gordon E. Richards, M.D., Toronto, Ont.

Roentgenological Manifestations of Allergic Processes in Pulmonary Tuberculosis. Max Pinner, M.D., Tucson, Arizona.

Public Health and Tuberculosis. Henry F. Vaughan, M.D., Detroit.

Case Findings. D. S. Brachman, M.D., Detroit.

Classification for Treatment. Bruce Douglas, M.D., Northville, Mich.

Pneumothorax in the Treatment of Tuberculosis. Richard Morgan, M.D., Detroit.

Surgical Procedures in the Treatment of Tuberculosis. E. J. O'Brien, M.D., Detroit.

Statistical Study of Detroit Department of Health Records. Henry F. Chadwick, M.D., Detroit.

WEDNESDAY AFTERNOON, SEPTEMBER 28, 1932

Symposium on Roentgenology in Gynecology and Obstetrics:

Pituitary Function as Related to Certain Uterine Problems. Robert C. Moehlig, M.D., Detroit.

Irradiation in the Treatment of Benign Conditions of the Uterus. George E. Pfahler, M.D., and Jacob H. Vastine, M.D., Philadelphia.

The Treatment of Malignancy of the Female Pelvis. William P. Healy, M.D., New York City.

Roentgen Evaluation of Breast Symptoms. I. H. Lockwood, M.D., Kansas City, Mo.

Further Cholecystographic Studies in the Late Months of Pregnancy. Lester Levyn, M.D., Edgar C. Beck, M.D., and A. H. Aaron, M.D., Buffalo, N. Y.

Results of Therapeutic Intrauterine Lipiodol Injection. H. P. Cushman, M.D., Detroit.

Roentgen Study as an Aid in Obstetrics. Henry J. Walton, M.D., Baltimore, Md.

WEDNESDAY EVENING, SEPTEMBER 28, 1932

Caldwell Lecture:

X-ray Findings and the Clinical Background. Kalamazoo, Mich. A. W. Crane, M.D., (Dr. Crane will be introduced by Dr. Henry Hulst of Grand Rapids, Mich.)

THURSDAY MORNING, SEPTEMBER 29, 1932

Congenital Absence of Superior Orbital Walls Associated with Pulsating Exophthalmus. Report of Two Cases. Lantern and Motion Picture Demonstration. Leon T. LeWald, M.D., New York City.

A Simplified Apparatus for Making Films of the Optic Canal. R. L. Pfeiffer, M.D., New York City.

The Roentgen Findings in Suppuration of the Petrous Apex. Henry K. Taylor, M.D., New York City.

Factors Influencing the Types of Metastatic Carcinoma of Bone. Elwood E. Downs, M.D., and Willard Hastings, M.D., Philadelphia.

Hypertrophy of the Pyloric Muscle and Duodenitis; Their Association and Roentgenological Manifestations. B. R. Kirklin, M.D., Rochester, Minn.

Roentgenologic Observations on the Evacuation of the Gallbladder. James T. Case, M.D., Chicago.

The Roentgen Demonstration of Non-Malignant Lesions of the Colon. Harry M. Weber, M.D., Rochester, Minn.

Roentgen Studies of Pulmonary Atelectasis. Willis F. Manges, M.D., and John T. Farrell, Jr., M.D., Philadelphia.

The Incidence of Malignancy in Chronic Prepyloric Gastric Ulcerations. Aubrey O. Hampton, M.D., Boston.

THURSDAY AFTERNOON, SEPTEMBER 29, 1932

The Relation of the American Society for the Control of Cancer to Roentgenologists. C. C. Little, Ph. D., Bar Harbor, Maine.

The Management of Carcinoma of the Urinary Tract. Rollin H. Stevens, M.D., and Harold Morris, M.D., Detroit.

Roentgen Therapy in Mammary Carcinoma. U. V. Portmann, M.D., Cleveland, Ohio.

Roentgen Irradiation in Malignancies of Bone. R. E. Herendeen, M.D., New York City.

The Roentgen Treatment of Pulmonary Malignancy. E. T. Leddy, M.D., Rochester, Minn.

The Therapy of Actinomycosis with Case Showing Lumbar Spine Involvement. Vincent W. Archer, M.D., University, Va.

Therapeutic Problems with Special Attention to High Voltage Technique.

Symposium on the Relative Effects Produced by 200 kv. X-rays, 700 kv. X-rays and Gamma Rays:

1. The Distribution of Radiation in a Water Phantom. G. Failla, E. H. Quimby, L. Marinelli, and J. E. Rose, New York City.
2. Comparisons Based on Some Chemical Effects Produced by the Three Qualities

of Radiation. H. Q. Woodward, H. R. Downes, and E. H. Quimby, New York City.

3. Comparisons Based on some Biological Changes Produced in the Lower Organisms. P. S. Henshaw, C. T. Henshaw, and D. S. Francis, New York City.
4. Comparisons Based on Some Biological Changes Produced in Mammalian Tissues. H. J. Bagg, and C. R. Halter, New York City.
5. Comparison Based on the Production of Erythema in the Human Skin. J. J. Duffy, R. F. P. McNattin, M. M. Copeland, and E. H. Quimby, New York City.
6. Comparison Based on Clinical Results. R. F. P. McNattin, New York City.
7. Correlation of Experimental Results. G. Failla, New York City.

THURSDAY EVENING, SEPTEMBER 29, 1932

Evening of Entertainment

FRIDAY, SEPTEMBER 30, 1932

Symposium on Malacic Diseases of Bones:

Max Ballin, M.D., and Plinn F. Morse, M.D., Detroit.

A. The Clinical Symptomatology of Osteomalacias (Including Calcium and Phosphorus Metabolism, Muscular Hypotonia).

B. Pathologic Classification.

C. Etiologic Classification (Hereditary, Nutritional, Endemic and Endocrine Factors).

D. Roentgenologic Grouping:

1. Rickets (Fetal, Infantile, Late). Ralph S. Bromer, M.D., Philadelphia.
2. Osteomalacia. Paul C. Hodges, M.D., and Alfred C. Ledoux, M.D., Chicago.
3. Primary Parathyroidism. E. R. Witwer, M.D., Detroit.

(a) Osteitis Fibrosa Cystica. Richard Dresser M.D., Boston.
Paget's Disease. Cornelius Dyke, M.D., New York City.
Leontiasis Ossea. Giant Cell Sarcoma. Carleton B. Peirce, M.D., Ann Arbor, Michigan.

(b) Ankylosing Polyarthritis of Oppel (Strümpell, Marie, Bechterew type) with Affections of Intervertebral Discs. E. W. Hall, M.D., Detroit.

(c) Doubtful (Osteopoikilosis). L. F. Wilcox, M.D., Detroit.
Marble-bone Disease; Kashin-Beck Disease. A. H. Pirie, M.D., Montreal.
Renal Rickets. E. C. Vogt, M.D., Boston.

4. Osteogenesis Imperfecta (Fragilitas Ossium). Ralph S. Bromer, M.D., Philadelphia.
5. Decalcification (in other Endocrine Disturbances).

(a) Graves' Disease and Thyroid Deficiency. Ross Golden, M.D., New York City.

(b) Diabetes (Islands of Langerhans). Ross Golden, M.D., New York City.

(c) Pituitary Origin (Basophile Adenoma). M. C. Sosman, M.D., Boston.

(d) Adrenal. Ross Golden, M.D., New York City.

6. Christian's Syndrome. Russell Rowland, M.D., Detroit.
7. Cooley's Syndrome. F. F. Borzell, M.D., and Emlen Stokes, M.D., Philadelphia.

Irradiation of the Parathyroids in Cystic Disease of the Bones. E. A. Merritt, M.D., Washington, D.C.

BOOK REVIEWS

Books Received Are Acknowledged under Heading: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers as space permits.

Pulmonary Tuberculosis. By Maurice Fishberg, M.D., Chief of the Tuberculosis Service, Montefiore Hospital, and of its Country Sanatorium for Incipient Tuberculosis. Volumes I and II. Fourth edition, thoroughly revised. Cloth. Price, $15.00. Pp. 1191, with 232 illustrations and 8 plates. Philadelphia: Lea and Febiger, 1932.

The new edition of Dr. Fishberg's textbook on "Pulmonary Tuberculosis" thoroughly modernized and largely rewritten, makes a fair bid to be what its predecessors were—the most useful English book on the subject for the general practitioner. Out of the various reasons for this statement, a few should be mentioned here: First, the author writes as a clinician for clinicians. Throughout his treatise, clinical standpoints and clinical problems occupy the center of the stage and pathology, epidemiology, bacteriology, roentgenology, and so on, are introduced as the auxiliary factors that they are in practical work. Second, the book presents, in thoroughly digested form, the advances which have been made in tuberculosis work during recent years. Scientific problems which according to current literature are still *sub judice*, such as filtrable forms of tubercle bacilli, BCG vaccination, etc., are fairly presented as problematical possibilities. Third, the book is eminently readable—an all too rare phenomenon in medical textbooks. Fourth, there is hardly a pertinent fact relating to its subject that cannot be found in the book.

But what has just been said about facts cannot be said about opinions. Dr. Fishberg has decided opinions on a number of important phases; these opinions are presented with the force of convictions. Dissenting votes, whether those of majorities or minorities, are much subdued or lacking. Dr. Fishberg may with some fairness be accused of the pecadillo of quoting or ignoring literature in too opportunistic a fashion, of using, or lightly brushing aside, statistics, as it may fit his aims. One senses that Dr. Fishberg was probably keenly aware of the difficulty of sailing safely between the Scylla of a scientific and thoroughly colorless textbook, and the Charybdis of a subjective message. Wherever the middle course is lost it deviates toward Charybdis. This accounts for overstatements. We suspect an over-zealous teaching attitude. It is difficult, because of such peculiarities, to render a completely fair review. There is probably not a single statement in the book which does not contain a large percentage of truth according to present knowledge. But there are many statements which call for protests because they are too absolute, too much 100 per cent. A few examples will illustrate the point. "It has been found [in experimental work] that reinfection is as difficult and even as impossible in tuberculosis as in syphilis." It would probably be a fair representation of the matter to say that under particularly favorable conditions of doses and interval between infection and reinfection, it is possible to show that infection may produce, at times, an almost complete immunity to reinfection. This point assumes great importance in Dr. Fishberg's work because it is one of the pillars on which he erects his theory—presented as a fact—that "Tuberculous infection can only occur once," with the logical corollary that protective measures against exogenous reinfection of adults are superfluous. Another example: the great stress that Dr. Fishberg puts on the careful evaluation of symptomatology is most commendable, but "*There is no active phthisis without fever, cough, tachycardia, languor, night-sweats, hemoptysis, etc.*" and "*If there are no symptoms of constitutional toxemia, the patient . . . is not sick. . . .*" (italics are the author's) are statements born undoubtedly of pedagogic zeal rather than of clinical wisdom. "A positive albumin reaction [in the sputum] is not always decisive of tuberculosis, but the negative outcome, when persistent during several examinations, undoubtedly excludes phthisis." "*. . . the absence of fever excludes active disease.*" That the author does not expect to be taken too literally may be concluded from the fact that a few pages later, cases of "apyretic tuberculosis" are discussed in some detail. In view of the fact that it is not an extremely rare occurrence to find a negative tuberculin reaction in an adult patient, the statement that the

tuberculin test "*in adults is of no clinical value at all*" should not go unchallenged.

These few examples of disagreement between Dr. Fishberg and facts are quoted not to point out factual errors, but to show the tendency to invalidate important points by exaggeration. Added to this weakness of strong convictions, Dr. Fishberg has certain opinions and points of view which are hardly representative of current (majority) opinions. It is to be highly commended that the work of Ranke is presented in some detail; his fundamental studies unfortunately have not received the attention in this country that they deserve. But the reviewer feels that Ranke's teachings are not adequately interpreted. The concept that tuberculosis evolves, not unlike syphilis, in three stages, is not original with Ranke, but was suggested long before him, by Petruschky. Ranke's essential work is the correllation of allergic, immunologic and histologic phenomena; according to him the stage is not characterized by a local lesion *per se*, but by the totality of the biologic reactivity; he taught, as it were, to read the immunologic state from the histologic picture. As indicated above, Dr. Fishberg's opinion on tuberculin, both in diagnosis and prognosis is at variance with that of many careful workers; they are appallingly radical on the negative side. Although the reviewer agrees fully with the author on the eminent importance of psychological influences, he should again classify the pronouncement "that tuberculin is of no therapeutic value whatsoever" as an unwarranted overstatement.

It was with deep disappointment that the writer read the chapters on collapse therapy. Since there can be no doubt that this book will influence many physicians, Dr. Fishberg's pessimism, far in excess of any justified scepticism, should have been labeled more clearly to be entirely his own. Although a fair number of authors are quoted in these chapters, it is decidedly the gloomy side that is presented. As far as the author's own experiences with pneumothorax are concerned, his hopelessness is probably largely explained by his advice: "*When we conclude that hygienic, dietetic, institutional and climatic treatment has been given a fair trial and that it has failed, therapeutic pneumothorax should be given serious consideration.*" This explains, no doubt, why "I have found less than 5 per cent of cases in which I could conscientiously urge this form of treatment, and of these at least one-third had sufficient pleural adhesions to render the attempt at collapsing the lung more or less futile." Or worse: "I am inclined to agree with those who hold that in less than 1 per cent of the total number of persons with active tuberculous disease of the lung is pneumothorax indicated." It seems only fair to remind the reader that the number of suitable candidates for collapse therapy is inversely proportionate to the number of missed opportunities. When pneumothorax is induced only after all other therapeutic endeavors have failed, success must be slight. The brief discussion of phrenicectomy is an over-pessimistic version of some of the reports with which the literature abounds, and the picture that is drawn of thoracoplasty and its results would suggest that this procedure has hardly a place in phthisiotherapy.

In view of the importance of the work, the adverse criticism of the previous paragraphs had to be stressed. Let it be said again that the criticism is not concerned with this or that detail that is mentioned as illustrative example, but with the method of pushing a point too hard, of selecting partial evidence suitable to support a subjective opinion, of lack of objectivity in the heat of an argument. It may be questioned, in fact, whether Dr. Fishberg's definiteness, and even dogmatism, does not increase the usefulness of his book for the general practitioner to whom it is mainly addressed. He who believes that the practising physician should be given full and unbiased information on facts and opinions will find Dr. Fishberg lacking here and there; he who thinks that the practitioner needs definite instructions upon which to act without the need of exercising his own critical powers, will think this book ideal. But, as stated in the beginning, the book as a whole has excellent qualities. Unlike many other books on the same subject, it gives a vivid picture of the tuberculous patient in all the protean features of the disease, it stresses impressively the necessity of considering the patient as a whole, it avoids the all too frequent tendency of getting lost in unessential details of technique and diagnostic fads. The chapters on symptomatology are particularly worth studying, as are those on diagnosis and on the various clinical forms of the disease. Here, the acute features are duly stressed. The significance of roentgenologic observation, including the frequently neglected roentgenoscopy, is pointed out, and a timely warning is given against attempts to diagnose a patient from the roent-

genogram only. Slight apical changes, demonstrable by physical signs and roentgenologic findings, are considered in detail. Recent studies have clearly shown that most of such lesions are clinically insignificant and that they are certainly not "incipient stages." Dr. Fishberg's discussion it is hoped, will go a long way to discourage overdiagnosing apical abnormalities that have nothing to do with active tuberculosis, and to draw further attention to the truly incipient infiltrative lesions whose signs and symptoms deviate so much from the traditional textbook teachings on incipient tuberculosis. The roentgenologist will be pleased with the many well-reproduced roentgenograms which are wisely chosen and authoritatively discussed. He will be interested in the author's scrutiny into the roentgenologic diagnosis of intestinal tuberculosis, which checked only in about 50 per cent of the cases with autopsy findings. He should carefully ponder over the chapter on "limitations of roentgenology" to realize that his method—indispensable as it is admittedly—is only *one* method in a complete examination, a method which can never replace clinical judgment in evaluating a patient's condition, nor bacteriologic findings in making an etiologic diagnosis.

In conclusion, Dr. Fishberg's book is recommended very highly; that this can be done conscientiously in spite of the defects that have been mentioned, speaks better for its quality than would unqualified praise.

Max Pinner

The Sign of Babinski. A study of the evolution of cortical dominance in primates. By John F. Fulton, Sterling Professor of Physiology in the Yale University School of Medicine, and Allen D. Keller, Professor of Physiology and Pharmacology in the School of Medicine, University of Alabama. Cloth. Price, $5.00. Pp. 165, with 65 illustrations. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1932.

The authors give the following as their reasons for the publication of a monograph on an isolated neurological sign: first, to emphasize the value of the higher primates for experimental studies on the central nervous system; second, to attempt a systematic comparison of human reflexes, normal and abnormal, with similar reactions in various primates below man; and third, as an experimental means of studying the evolution of the human brain.

The most important part of the original description of the sign of Babinski which appeared in *La semaine medicale* in 1898 is reproduced with a translation of the first few paragraphs. The authors state that this sign is now generally recognized as specific evidence of injury to the pyramidal paths, but that the underlying mechanism of its production is unknown and that an experimental analysis has not previously been attempted in lower animals. They direct attention to the observations on man which suggest that "the suppression of activity of the higher centers of the nervous system give rise to the sign of Babinski." This is supported by the evidence that the sign becomes positive during the stage of apnea in Cheyne-Stokes respirations and tends to be positive during normal sleep.

The main part of the book consists of a series of careful original observations on the Babinski sign following the production of experimental surgical lesions in the central nervous system of the higher primates. A series of these animals were studied thoroughly, including the monkey, baboon, gibbon and chimpanzee, and an analysis and comparison of the results in these various animals is discussed. Among other conclusions the authors state "that in the higher primates the sign of Babinski is associated with isolated destruction of the pyramidal pathways. No one has demonstrated its presence unequivocally in extrapyramidal lesions of the nervous system."

A very helpful appendix is added by Dr. Fulton concerning the surgical technique, after care and anesthesia which is useful in experimental neurosurgery.

The book is an excellent presentation of a specialized subject for the neurosurgeon and the student of neurology, but will not appeal especially to undergraduate medical students or practitioners.

C. C. Sturgis

California's Medical Story. By Henry Harris, M. D., Associate Clinical Professor of Medicine, University of California; Chief of Medical Department of San Francisco Polyclinic. Pp. 421. San Francisco: Printed by the Grabhorn Press for J. W. Stacey, Inc., 1932.

This work is an interesting, well written and a thorough contribution from California to the medical history of the United States. The author has apparently devoted a great deal of

time and painstaking care to the investigation of many important as well as minute facts concerning the development of medicine in that state. He has logically divided the material into the following sections: The Medicine of the California Indian, Spanish Period, Mexican Period, the American Period—Acquisition, Organization, Progress, Practice and Biography.

One is fascinated by the story of the doctors of the Gold Fever time, a colorful part of the history of the state. According to the author, between 1300 and 1500 doctor adventurers came to California with the gold seekers. "It is the flotsam and jetsam of medicine that comes; the ignorant and the educated, the bombastic and the modest, the rogue and the champion of righteousness, the irresponsible and the trustworthy, the fool and the philosopher, the worst and the best." Following these came the younger generation, the native sons, who were destined in later years to establish the practice of medicine on a firm basis in the state. Among these was Robert Armisted McLean, the first boy born in Stockton and the first native son to receive a medical degree from a local school (Toland College). He later became Dean and Professor of Clinical Medicine in a school of his native state. Also there was Joseph Oakland Hirschfelder, the first child born in Oakland of white parents, who graduated from Leipzig in Medicine and later became Professor of Clinical Medicine at Cooper College.

The book is replete with interesting descriptions of the development of medical education, the formation of the state societies, the creation and progress of the medical press, the plague, the Chinese doctors, and the evolution of hospitals. The author has an interesting statement concerning medical quackery even down to Dr. Albert Abrams whom he characterizes as "A tangental colleage possessing the boastfulness of Paracelsus, the self-deception of the alchemists, the alertness, tenacity and ruthlessness of the robber barons."

Dr. Harris is to be congratulated upon the production of California's Medical Story for it appears to be a very readable as well as an authentic and complete account of the development of medicine in that great state.

C. C. Sturgis

Books Received

Fungous Diseases: A Clinico-Mycological Text. By Harry P. Jacobson, M.D., Attending Dermatologist and Member of the Malignancy Board, Los Angeles County General Hospital. With introductions by Jay Frank Schamberg, M.D., Professor of Dermatology and Syphilology, Graduate School of Medicine, University of Pennsylvania, and Howard Morrow, M.D., Clinical Professor of Dermatology, University of California Medical School. Cloth. Price, $5.50. Pp. 317, with 153 illustrations. Springfield, Illinois: Charles C Thomas, 1932.

Allgemeine und spezielle Elektrochirurgie. Von Dr. Med. Hans V. Seemen, Privatdozent für Chirurgie an der Universität München, Oberarzt an der Klinik Lexer. Mit einem Beitrag Elektrochirurgie der Geschwülste in Verbindung mit Strahlenbehandlung von Dr. Med. Otto Schürch, Privatdozent für Chirurgie an der Universität Zurich, Oberarzt an der Klinik Clairmont. Paper, price RM 62.00; bound, RM 66.80. Pp. 474, with 347 illustrations.

A Descriptive Atlas of Radiographs: An aid to modern clinical methods. By A. P. Bertwistle, M.D., Ch.B., F.R.C.S. Ed. Second edition, revised and enlarged. Cloth. Price, $13.50. Pp. 552, with 767 illustrations. St. Louis: C. V. Mosby Company, 1932.

Eine Methode zur Messung von Röntgen-Radium- und Ultrastrahlung nebst einige Untersuchungen über die Anwendbarkeit derselben in der Physik und der Medizin. Mit einem Anhang enthaltend einige Formeln und Tabellen für die Berechung der Intensitätsverteilung bei ψ-Strahlungsquellen. (*Acta radiol., Suppl.* xiv.) Von Rolf M. Sievert. Paper. Price, 20 Swed. crowns. Pp. 179, with 63 illustrations. Stockholm: P. A. Norstedt & Söner, 1932.

A Study of the Ionization Method for Measuring the Intensity and Absorption of Roentgen Rays and of the Efficiency of Different Filters Used in Therapy. (*Acta radiol., Suppl.* xv.) By Robert Thoraeus. Paper. Price, 10 Swed. crowns. Pp. 88, with 40 illustrations. Stockholm: F. Englunds, 1932.

How Children Grow: An anthropometric study of private school children from two to eight years of age. By Ruth Sawtell Wallis, Ph.D. University of Iowa Studies, August 1, 1931, 5, pp. 137.

Proceedings of the Annual Congress of Medical Education, Medical Licensure and Hospitals. Chicago, February 15 and 16, 1932. Pp. 123. Chicago: American Medical Association, 1932.

Report of the Royal Commission on the Use of Radium and X-Rays in the Treatment of the Sick, etc. Pp. 171. Toronto: Herbert H. Ball, 1932.

Annual Report. 1931. The Radium Institute, London, Pp. 67, with 3 illustrations.

DEPARTMENT OF TECHNIQUE

Department Editor: Robert B. Taft, 105 Rutledge Ave., Charleston, S. C.

A CASSETTE WITH A CONVEX CURVE

By R. D. LEONARD, M.D., *and* A. W. GEORGE, M.D.
BOSTON, MASSACHUSETTS

WE HAVE found a curved cassette of considerable value in obtaining unusual views of various parts of the body. The idea of a curved film holder is not new. For years this method has been used by us in lateral views of the cervical spine and other conditions.

Lately, we have found this type of film holder of value in the study of fractures of the neck of the femur. As most of these fractures are treated with the leg in abduction, it has been possible to obtain vertical views of the femoral neck with a curved film holder. This is shown in Figure 6. On account of the thickness of the parts, we had constructed a curved cassette which allows the use of double intensifying screens (see Fig. 4).

This view of the neck of the femur gives us accurate information as to the degree of apposition of the fragments. Figure 6 shows the relative position of the tube and cassette for obtaining the vertical view of the femoral neck.

We have found this cassette of value, not only in the study of fractures of the neck of the femur, but also for the study of the base of the skull. As is shown in Figures 2 and 3, the entire foramen magnum is easily demonstrated. Fractures involving the edges of the foramen are demonstrable, as shown in Figure 3.

Fig. 1. Showing a curved cassette in position for roentgenographing the occipital bone in the region of the foramen magnum.

Fig. 2. Demonstration of foramen magnum. This film was obtained by position shown in Figure 1.

Fig. 3. Demonstration of a linear fracture of the occipital bone extending into the foramen magnum.

In studying the base of the skull, we also noted that valuable views could be obtained of the condyle and joints of the lower jaw and also the outline of the sphenoid sinuses (see Fig. 5).

Fig. 5. Film obtained in the position shown in Figure 4, showing the sphenoid sinus and the condyles and joints of the lower jaw.

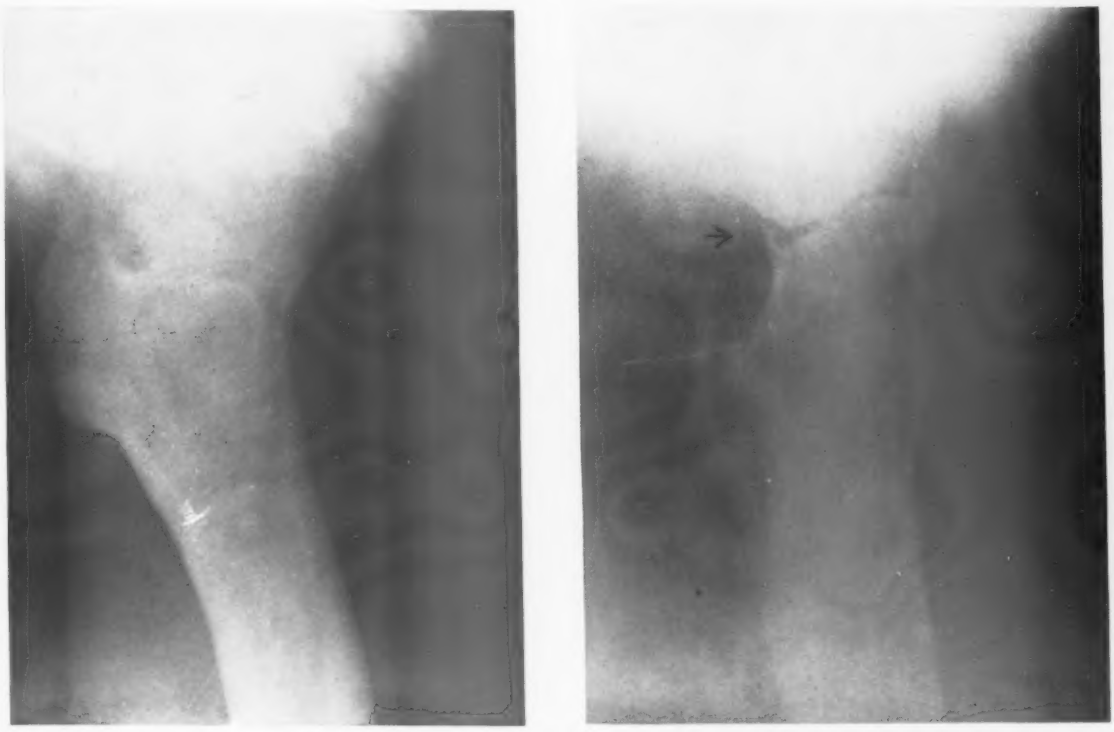
The cassette which we are using takes a 10″ by 12″ film. The point of greatest convexity is about 4 inches from the horizontal plate. Only the central portion of the exposed film is of value. The shadows on the ends of the film are considerably distorted due to the curvature.

Fig. 4. Curved cassette in position for obtaining views of the anterior portion of the base of the skull and lower jaw.

Fig. 6. Diagram showing the position of the cassette and roentgen tube for obtaining a vertical view of the neck of the femur. In this view the patient is lying on the back with the leg abducted, the cassette standing on end.

This type of curved cassette may be useful in many other problems, and with fur-

ther experience the technical quality of the films will be improved. A cassette of this type should be a useful adjunct to the office of any roentgenologist.



A B

Fig. 7. Vertical views of the neck of the femur made in the position shown in Figure 6. A—Showing a fracture with rotation of the shaft. Poor apposition. B—Same case after reduction with the fragments in good apposition.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

SKELETAL SYSTEM

KEY, J. ALBERT. Experimental arthritis; the changes in joints produced by creating defects in the articular cartilage. *J. Bone & Joint Surg.*, Oct., 1931, *13*, 725–739.

The cause of chronic arthritis is unknown. Some of the theories of its causation are as follows: Axhausen, pathologic changes of chronic arthritis, hypertrophic type, are due to the presence of dead cartilage within the joint; Wollenberg, a vascular theory, production of degenerative and hypertrophic changes by interference with blood supply; Axhausen (later experiments), production of the same changes by killing a portion of cartilage in the opened joint by cautery, the joints being thereupon closed and after a period of months, development of typical changes; Burckhardt, experiments on a series of guinea pigs, opening the joint and placing a drop of carbolic acid or iodine within it, closure of the joints, some of which were immobilized and others were used normally by the animals. In the used joints the pathological changes characteristic of arthritis deformans developed in from three to five months, while in the joints which were immobilized the cartilage remained intact for a long time and then was gradually replaced by connective tissue and new cartilage which in some instances caused the joint to be filled with a cartilaginous connective tissue and tended to produce ankylosis with a picture resembling that of atrophic or infectious arthritis.

In this paper Key reports the changes produced in the joints of rabbits by the aseptic removal of a portion of cartilage. His experiments prove that many of the changes which occur in hypertrophic arthritis can be produced experimentally in the joints of rabbits by simply creating a defect in the cartilage and that these changes are not dependent upon the presence of dead cartilage within the joint, unless one assumes that the small amount of cartilage necrosis around the borders of the defect is the cause of the arthritis, and this, he considers would be ridiculous. However, in order to determine whether or not the presence of dead cartilage within a joint produced arthritis, in a few instances he removed articular cartilage from the surface of one knee, boiled it, and then inserted it into the cavity of the opposite knee. The dead cartilage became adherent to the fat pad and was gradually destroyed and no arthritis developed in the joint.

In studying the joints of his series of rabbits, he was not able to determine the nature of the stimulus to new bone formation; but in going over the sections, he was impressed by the fact that the bone marrow in the lower end of the femur in the joints which developed well-marked arthritic changes appeared to be unusually vascular and that the blood vessels were larger as well as more numerous than normal. Whether this increased vascularity in the bone marrow is the result of the removal of the cartilage and the exposure of the underlying bone, or whether it is the result of the proliferative changes which occurred in the bone he was not able to determine.

He noted that the incision in the cartilage or bone which caused a cut surface to be exposed to the synovial fluid in the joint always resulted in the death of the cartilage or bone cells adjacent to this surface. Yet there is no evidence that in simple fractures the ends of the fragments are ever sequestrated or even absorbed after union occurs. Somewhat the same thing occurs in the surface of bone which is exposed in a joint by the removal of the articular cartilage. This bone may persist for a long time without being covered by new tissue and may become eburnated by the deposition of new bone in the adjacent marrow spaces, or it may become covered by cartilage or fibrous tissue, and in animals of Willis' series this tissue seemed to become adherent to the apparently dead bone which persisted in situ over a period of six or seven months.

The cause of the softening and wearing away of the cartilage on the bearing surface of the femur and tibia, Willis states, also remains obscure, as these changes occurred in joints in which there was not enough deformity to explain them by increased mechanical work. Likewise he can not explain the hypertrophy of the margins of the tibia and patella and the laying down of new subperiosteal bone around the upper portion of the shaft of the tibia.

He noted that several types of reaction might result from the same type of injury. He could not find any reason for a given type of change in these joints. The factor of infection was ruled out by opening the joints under aseptic conditions and culturing small bits of synovial membrane. It appeared that if two joints were subjected to practically identical operative procedures, one may return to a practically normal condition and the defect may be healed by cartilage which approaches the normal articular cartilage, and there may be no reaction in the bone or joint except the deposition of a very small amount of subperiosteal bone on the sides of the femur; while in the other joint a condition resembling severe hypertrophic arthritis may develop. What the factor is that determines which process will occur has not been revealed by these experiments.—*R. S. Bromer.*

Weissenbach, R.-J., and Truchot, P. Calcifications périarticulaires et ossification, type Pellegrini-Stieda de la région de l'épaule, après traumatisme. (Periarticular calcifications and ossification, Pellegrini-Stieda type, of the shoulder region after traumatism.) *Bull. et mém. Soc. méd. de hôp. de Par.*, Nov. 30, 1931, *55*, 1790–1793.

The case reported is a rare example of two types of traumatic sequelae about a joint: periarticular calcification and the ossification of Pellegrini-Stieda. Strictly speaking, this ossification refers to that about the internal condyle of the femur following trauma, but the term is used in the wider sense as applying to any joint.

The patient injured his shoulder thirty years ago. A stereoscopic roentgenogram showed a mass like a cap topping at a distance, the head of the humerus, with hollowing of the external part through which passes the tendon of the supraspinatus. It lay between the deltoid and the scapulo-humeral articulation. This mass of periarticular calcification is dense, rough and has a winding contour. On the inside of the internal border of the humerus at the inferior and posterior part of the joint there is an ovoid mass with very regular borders, of great opacity, homogeneous. It has the appearance of an osteoma.

Some periarticular calcifications are associated with trauma; calcareous infiltration of connective tissue or organized hematoma. Others are independent of trauma; fibrous periarthritis, metabolic disturbance of connective tissue as in scleroderma, static arthritis.—*Ellsworth Johnson.*

Rouillard, J., and Bousser, J. Ossification du ligament latéral interne du genou. Maladie de Pellegrini-Stieda? (Ossification of the internal lateral ligament of the knee. Pellegrini-Stieda's disease?) *Bull. et mém. Soc.*

méd. de hôp. de Par., Nov. 23, 1931, *55*, 1739–1744.

Pathological ossification in the neighborhood of the internal condyle of the femur is known as Pellegrini-Stieda's disease. It usually occurs in adult males following trauma to the knee. This trauma, while it may be slight, is most often severe.

The shadow on the roentgenogram is situated about the internal condyle with the borders more or less parallel. It may lie a short distance from the condyle or be attached to the bone. The recent formations appear free while the old ones tend to be fastened to the condyle. It may appear decalcified.

It is difficult to know if the bony fragment was pulled off from the epicondyle or if it represents an ossification of the internal lateral ligament; the latter is the generally accepted view.

A case is presented in which the etiology is complex. It is illustrated by two roentgenograms.—*Ellsworth Johnson.*

Sundt, Halfdan. The diagnosis and frequency of tuberculous disease of the knee. *J. Bone & Joint Surg.*, Oct., 1931, *13*, 740–758.

The author's experience covers 310 patients suffering from affections of the knee joint, admitted during nineteen years, 1911–1930, to the Coast Hospital, Stavern, Norway. Of these, 205 (66.1 per cent) were found to be suffering from tuberculosis, while 105 (33.9 per cent) were undoubtedly, or in all probability, not suffering from tuberculosis in the joint. He states that when dealing with a tuberculous affection of the knee, every one of our diagnostic methods may play us false in a given case. The clinical picture presented by a tuberculosis of the knee joint is usually either that of a fungus, tumor albus genus, or a hydrops chronicus genus, or both of these.

The most convenient method of deciding the diagnosis of a hydrops genus, is of course, inoculation from a puncture into guinea pigs. This however does not always hold good. The guinea pig test in his series failed in 25 per cent of 32 negative cases. In regard to the tuberculin test, the positive von Pirquet reaction has an important significance only in the very first years of life—up to the age of three or four years. In a child of this age with a tumor albus or hydrops, when other infection can be ruled out, a positive von Pirquet reaction will decide the diagnosis with a degree of probability bordering upon certainty. As the years increase, the positive cutaneous reaction will lose in value as a diagnostic aid and will be entirely devoid of significance when the age limit is passed, at which 50 per cent of the population gives a positive reaction. A negative von Pirquet does not exclude the existence of an active bone or joint tuberculosis. The only convincing proofs are, on the one hand, the absolutely negative result of all tuberculin tests up to 10 mg. and, on the other hand, a focal reaction that both objectively and subjectively is undoubtedly positive. In surgical tuberculosis such a reaction is, however, as rare as it is capricious. Producing a focal reaction in Pirquet-positive individuals by means of subcutaneous injections in increasing doses, is not entirely devoid of danger. Of late years, too, focal reactions have been produced by the injection of nonspecific proteins, such as typhus vaccine, milk, etc.

Sundt believes the value of the roentgen examination in bone and joint tuberculosis has long been overestimated. It is a known fact that an entirely negative roentgen finding does not preclude the possibility of tuberculosis in a joint, and on the other hand, a roentgen picture that is usually regarded as characteristic for joint tuberculosis affords no absolutely decisive proof of its presence. The periosteal deposits which are regarded as indicative of syphilis or osteomyelitis and contraindicative of tuberculosis, can occur in the latter, especially in cases having old fistulae, and also in cases not solely affecting the diaphysis.

He concludes that no roentgen picture exists that is entirely typical of joint tuberculosis in any of its stages. The evenly diffused calcium atrophy, which was at one time regarded as so characteristic of tuberculous arthritis, is a phenomenon present in all joint infections in which the synovia are attacked. It is also found in syphilitic lesions. It cannot be regarded as pathognomonic of tuberculosis. Again, the spotted calcium atrophy which was regarded as typical of chronic nonspecific arthritis can occur in tuberculous arthritis. Uneven contours of joint margins of bones may occur likewise in other conditions. The roentgen diagnosis is often rendered more difficult by the fact that extensive osseous changes, sequestra, etc., may fail to appear in the roentgenogram, inasmuch as they are just as poor in calcium as their surroundings, thus being invisible on the

film. It is a common experience to find destructive joint changes at operation which previously gave no roentgen evidence. Even if foci are revealed in the roentgenogram, the latter gives no proof of the nature of the osseous change. He quotes König: "We cannot practice pathological anatomy with the roentgen plate."

In summing up the value of the sedimentation test, he concludes that it has not enriched the diagnostic armamentarium of surgical tuberculosis. It is not entirely useless as he admits that an excessively high sedimentation rate speaks for osteomyelitis rather than for tuberculosis.

He thinks the complement-fixation test (tuberculosis Wassermann reaction) is unreliable and even misleading, whether made in fluid from aspirated cold abscesses or in blood. A negative reaction in the puncture fluid is entirely without diagnostic significance. A decidedly positive (two plus) reaction in the puncture fluid, or a more strongly positive reaction in it than in the blood, must be regarded as decisive just as is the case with the Wassermann reaction in arthritic lues.

The remainder of his paper contains a discussion of exploratory arthrotomy with special reference to its diagnostic significance. In addition, he exhaustively reviews his cases from the standpoint of differential diagnosis. His non-tuberculous cases consisted of arthritis deformans, pyogenic, hemophilic, luetic, and hysterical arthritis. He includes in his series one case of chondrosarcoma of giant cell type, one of xanthosarcoma of giant cell type, three of osteochondritis dissecans, one of chondromatosis of the patella, and 55 cases of uncertain origin. The latter consisted of 5 cases probably syphilitic in origin, a number of cases of traumatic origin, traumatic synovitis, and a number of cases of an indolent hydrops of the knee, occurring in both adults and children and not of syphilitic origin. He believes that in cases which could be included in the category of Poncet's "tuberculose inflammatoire" (so-called tuberculous rheumatism), tuberculosis must be considered as a possible cause, provided no infection nor any other cause for these mono- or polyarticular types of joint changes can be found.—*R. S. Bromer.*

Christopher, Frederick. Fracture of the anterior process of the calcaneus. *J. Bone & Joint Surg.*, Oct., 1931, *13*, 877–879.

Christopher reports 3 cases of fracture of the anterior process of the calcaneus. He thinks the injury is common and at the time of writing this paper no previous reports or description of the fracture could be found. Since then an article by Dachtler appeared in the *American Journal of Roentgenology and Radium Therapy*, May, 1931, which Christopher cites in a footnote. The injury is easily demonstrated in roentgenograms, and is probably caused by forcible plantar-flexion of the foot. The treatment recommended by Christopher is immobilization in a circular plaster cast for three or four weeks followed by physiotherapy.—*R. S. Bromer.*

Shaffer, Loren W. Subungual exostoses. *Arch. Dermat. & Syph.*, Sept., 1931, *24*, 371–379.

This curious disease is described, and 4 cases are reported. Subungual exostoses are not rare. They are solitary, benign, painful tumors, the size of a pea, occurring beneath the inner margin of the great toe nail. These exostoses very often occur on the little toe, and rarely on the fingers. Arising from a cartilaginous outgrowth they later become osseous. These tumors are three times as common in women as in men and usually appear between the ages of twelve and thirty. If not completely removed recurrence takes place.

The greatest difficulty in roentgen diagnosis arises from early cases in which ossification has not occurred. These early immature or cartilaginous forms may present negative roentgenologic observations, or there may be a faint shadow of early cartilaginous exostoses. In the intermediate type the exostoses do not show the sharp outline that is found in the mature form. Besides having a sharply defined bony exostosis which has been deflected anteriorly, the mature form may have a faint outline of the nodule.—*Ellsworth Johnson.*

BLOOD AND LYMPH SYSTEM

Pearse, Herman E., Jr., and Warren, Stafford L. The roentgenographic visualization of the arteries of the extremities in peripheral vascular disease. *Ann. Surg.*, Dec., 1931, *94*, 1094–1102.

The condition of the lumen of the vessels of the extremities is of importance in peripheral vascular disease. Heretofore any injected radiopaque substance caused injurious effects, especially if the vessels were already markedly

diseased. Because of the tolerance of the body for large doses of methiodol (skiodan) in intravenous pyelography, this substance was selected. It is sufficiently radiopaque to visualize the vessels in concentrations low enough to be harmless to the vessel walls. This last point was determined by injections into the arteries of lower animals, after which the artery was examined for histologic evidence of harmful effects. The authors use a 40 per cent solution of methiodol in freshly distilled water, sterilized by boiling. The artery is exposed under local anesthesia and is compressed with the finger. The needle of a 50 c.c. syringe is plunged obliquely through the vessel wall and 25 c.c. of the solution injected. A film is taken immediately. The remaining 25 c.c. of solution is then injected and a film is exposed during the injection. There is very little bleeding on removing the needle. The authors report 7 cases. In 5 the extremity was amputated. No evidence of injury to the vessels by the solution could be found. The procedure gives promise of offering a useful addition to the study of peripheral vascular diseases.—*M. T. Harris.*

GENERAL

WEISSENBACH, R.-J., TRUCHOT, P., FRANÇN,O F., and LAUDAT M. Rhymatisme chronique fibreux, sclerodérmie et concrétions calcaires sous-cutanées. Etude radiologique et biochimique. (Chronic fibrous rheumatism, scleroderma and subcutaneous calcareous concretions. Roentgen and biochemical study.) *Bull. et mém. Soc. méd. de hôp. de Par.*, May 25, 1931, *55*, 837–847.

This is a lengthy report of a case of chronic fibrous rheumatism of thirty years' standing, and of calcareous subcutaneous concretions of fingers and left elbow, with sclerodermic thickening of skin of the face, which was first noticed three years before. Roentgen examination of the hands and fingers revealed a small mass of calcareous concretions with regular contours at the end of the right thumb; along the phalanx of the right index finger were unequal and irregular deposits of fine granules. The right elbow showed limited linear deposits in the tendon of the triceps, while the left showed long, irregular, thick shadows in the tendon of the triceps almost in contact with the olecranon.

The authors conclude that the elevation of blood calcium does not explain the precipitation of calcium salts in the tissues, and that the local changes of physicochemical tissue affinity play a leading and probably exclusive rôle in many cases Two illustrations are presented.—*Ellsworth Johnson.*

MOUCHET, A., and ROEDERER, C. Chirurgie infantile et orthopedie en 1931. (Infantile surgery and orthopedics in 1931.) *Paris méd.*, July 18, 1931, *2*, 53–71.

In this general review the authors discuss orthopedic and surgical conditions of the vertebral column, extremities, face, abdomen and pelvis. Some generalities as spinal anesthesia and roentgenography after injection of lipiodol are included, as well as diseases of the bones and muscles, congenital malformations, and the apparatus used for treating the sequelae of polyomyelitis.

Kümmell-Verneuil's syndrome or traumatic spondylitis is discussed. In Pott's disease laminectomy was performed when paraplegia was present. Other vertebral affections mentioned are infantile vertebral osteochondritis, spondylolisthesis, sacralization of the fifth lumbar vertebra, spinal echinococcus cyst, nucleus pulposus, kyphoses of adolescents, and incontinence due to compression of dural cul-de-sac by a fibrous extradural core or stone.

Congenital dislocation of the hip, coxalgia, coxa vara, and other diseases of the hip are cited. In discussing diseases of the knee, tuberculosis of the knee as well as of the patella is included. Congenital dislocation of the knee and patella is mentioned; also Pellegrini-Stieda's disease, traumatic lipo-arthritis of the knee, and Schlatter's disease. The diseases of the feet mentioned are hallux varus, congenital club foot, tuberculosis, osteomyelitis of the scaphoid, subluxation of the astragalus, and Dupuytren's fracture. Included in diseases of the upper extremity are obstetrical paralysis, osteochondritis of the shoulder, tuberculous osteitis of the humerus, congenital ankylosis of the elbow, and fracture of the carpus.

Megacolon, acute intussusception in infants, and osteomyelitis of the pubis are included in diseases of the abdomen and pelvis.

The triad of symptoms of Schüller's disease is cited, as well as a number of other diseases of the bones.—*Ellsworth Johnson.*

FIGI, FREDERICK A., and CUTTS, ROLLIN E. Actinomycosis in childhood. *Am. J. Dis. Child.*, Aug., 1931, *42*, 279–290.

In the human, actinomycosis is primarily a disease of early adult life. Many textbooks on

pediatrics do not even mention the disease, and those that include it give only meager descriptions. In most of the reported cases of the infection in children, the disease was well advanced when recognized clinically and with few exceptions it progressed to a fatal termination. Figi and Cutts report 14 cases of actinomycosis from the Mayo Clinic. The ages of the children affected ranged from two to fifteen years.

The clinical history, symptoms, physical conditions, diagnosis and treatment of actinomycosis in children are similar to those related to the infection in adults. The children in this series comprised a little less than 3 per cent of approximately 450 patients with actinomycosis examined in the Mayo Clinic; 9 of them were boys and 5 were girls. The cervico-facial area was involved in 10 cases, and the abdomen in 4 cases. In 2 of the latter the infection was first evident in the lumbar region.

An outstanding point of difference in the histories of children and adults was the absence of previous trauma in the latter group. A history of dental extractions or penetration of the oral or pharyngeal mucous membrane with grain beards and grasses, which so commonly precedes the onset of the disease in adults and obviously furnishes the portal of entry for the infection, was conspicuously absent in the children. Some of the children had repeated attacks of sore throat before the onset. Several had carious teeth and diseased tonsils which may have been etiologic factors. The mode of onset and the course of the disease varied somewhat with the site of the infection and its virulence, as has been repeatedly observed in adults. The usual sequence of the cervico-facial lesions was the development of a definitely circumscribed, indurated, tender swelling, usually in the cheek, parotid gland or submaxillary region, accompanied or followed by dull aching or acute pain, and later by the appearance of redness of the skin, and fluctuation. In all the deep-seated lesions about the head, trismus or ankylosis of varying degree was an early symptom. In all the abdominal cases the systemic symptoms were pronounced. Two such cases followed appendectomy. Sinuses were present in all the abdominal cases. The duration of symptoms prior to registration at the Clinic varied from four weeks to thirteen months in the cervical cases. In the abdominal cases, symptoms had been present for eight months to five and one-half years.

Actinomycosis must be considered as a diagnostic possibility with regard to indeterminate tumor, chronic infection or persistent sinus, even if the patients are young. Freshly drained pockets offer a better opportunity for demonstrating the fungus than sinuses which have been draining for a long time. After suppuration has occurred, the clinical picture is so characteristic that the condition may frequently be recognized at the time the patient is first seen.

The treatment of the cases of this series consisted of saturated solution of potassium iodide internally, beginning with from 4 to 5 minims, three times daily, and gradually increasing one drop daily or every second day to the point of tolerance. Radium was administered with distance and screening over the affected area at intervals of from three to six weeks, as long as there was evidence of active infection. The number of treatments with radium given in any individual case varied from one to five. From 2,000 to 6,000 milligram-hours, using 2 mm. of lead screening and a block of wood 2.5 cm. thick for distance, was given at each application. In a few instances in lieu of this, the patients received deep roentgen therapy with apparently equally beneficial results. Continuous hot, moist compresses were also used over the area affected and free drainage was established as soon as suppuration occurred.

The prognosis in cases of actinomycosis in children, as in cases in adults, varies with the site, extent and virulence of the infection. In cases in which the head and neck are affected, the outlook for cure is good, unless the infection is unusually virulent and extensive, or there is evidence of intracranial or intrathoracic extension at the time treatment is instituted. In the abdominal and thoracic cases the prognosis is, as a rule, poor. Of the 10 children of this series with infection of the head and neck, 8 are alive and well. Three of the patients with abdominal actinomycosis are dead.—*R. S. Bromer.*

ROENTGEN AND RADIUM THERAPY

Dyke, Cornelius G., and Goss, Sidney W. The roentgenotherapy of pituitary tumors. *Bull. Neurol. Inst. N. York*, June, 1931, *1*, 211–228.

The clinical records of 5 patients are presented in whom a diagnosis of pituitary neoplasm was made and who were treated by roentgen therapy. The cases were followed from six to twelve months after beginning treatment.

In every case the headache was entirely relieved. In 3 patients marked improvement in the visual fields and visual acuity resulted; the other 2 showed no further loss of vision. All were markedly improved subjectively.

The factors used were: 155 kv. (constant potential), 1 mm. aluminum plus 0.5 mm. copper filter; 20 inch distance; 4 ma.; 83 minutes; which equals 800 r (international). The patients are irradiated through three 10 cm. portals, that is, both temporal regions and forehead. One portal is treated every other day, giving a dosage of 250 r. If no untoward symptoms are noted after four such treatments, they are given daily thereafter. The temporal area receives a total of 750 r and the frontal area 500 r. This is considered one series and every case is given four or more series at six weeks' intervals. The visual fields are charted after each roentgen treatment as this is the best guide to the patient's reaction to treatment. The authors state they realize that this is a small series of cases and the time is relatively short but they believe the results warrant a further trial of roentgen therapy.—*R. R. Rathbone.*

Cappelli, Luigi. I primi rilievi clinico-biologici nell'applicazione del criterio "radioamitogeno." (First clinical and biological results in the application of radio-amitosis.) *Radiol. med.*, Oct., 1931, *18*, 1352–1362.

The author thinks that in the treatment of malignant tumors it is preferable not to attempt to kill the tumor cells but to destroy their capacity for karyokinesis. This method he calls radio-amitosis. The capacity of the tumor cells for reproduction is destroyed and they are then absorbed by the natural forces of the body. This method consists in reducing the dosage and prolonging the time of treatment. With radium, instead of the dose of 10–50 or more milligrams formerly used, he uses 1–6 milligrams but applies it uninterruptedly for 9–10 weeks. He describes his results in 30 basal celled tumors, most of them radioresistant. Not only did histological examination show arrest of karyokinesis, but clinically the tumors stopped growing and decreased in size, some of them disappearing completely. This demonstrates more conclusively than histological examination that they had lost their capacity for growth. The action is specific and the normal tissues are not injured at all. On the contrary, there is improvement in the blood picture and general health even during the course of the treatment.—*Audrey G. Morgan.*

ACTION OF ROENTGEN RAYS AND RADIUM

ON THE

HEART AND LUNGS

EXPERIMENTAL DATA AND CLINICAL RADIOTHERAPY

BY

A. U. DESJARDINS

MAYO CLINIC

ROCHESTER, MINNESOTA

SECTION FIVE

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ACTION OF ROENTGEN RAYS AND RADIUM ON THE HEART AND LUNGS

LUNGS

General Considerations

Most of the early investigations of the action of roentgen rays on various organs had not revealed any perceptible influence of irradiation on the lungs, and until recent years instances of clinical injury to the pulmonary apparatus had never been recorded. These reasons undoubtedly accounted for the general impression that the pleura and lungs were not very sensitive to roentgen or radium radiation. With the advent of roentgen rays of short wave-length and the use of maximal doses in the treatment of different varieties of malignant neoplasms, however, it soon became apparent that, while the pleura and lungs are not especially vulnerable and can tolerate ordinary therapeutic doses, their radiosensitiveness is distinctly greater than that of certain other organs, such as the heart and liver, and extreme therapeutic irradiation of the thorax may lead to inflammatory reaction. This had been well shown by the experiments of BERGONIÉ and TESSIER (1898), but their demonstration had been an accidental by-product of investigations the object of which was to determine the action of roentgen rays on pulmonary tuberculosis. This probably explains why such a valuable fact should have failed to attract attention at the time and should have been completely lost from sight. Since then, several investigators have attempted to elucidate the problem.

Animal Experiments

Roentgen Rays. BERGONIÉ and TESSIER (1898) inoculated six guinea pigs of about equal weight by injecting into the right pleural cavity one-fourth cubic centimeter of a concentrated dilution in sterile distilled water of a month-old culture of human *Bacillus tuberculosis* of medium virulence. From twenty-four to forty-eight hours later, the entire body of three of the guinea pigs was exposed to roentgen rays[116] for thirty minutes daily or every second day. At first the animals were immobilized on a board, but later they were kept, during irradiation, in thin boxes of wood or cardboard. Trophic lesions were not observed, but the animals irradiated for a long time became temporarily apathetic and drowsy. The three other animals were not exposed to the rays but were kept as controls. Under these experimental conditions, all the guinea pigs lost weight, but this loss was greater in the irradiated than in the unirradiated animals. The animals exposed to roentgen rays died twenty-two, sixteen, and fifteen days, respectively, after inoculation. The controls died twenty-one, thirty-six (killed), and thirteen days, respectively, after inoculation. The irradiated guinea pigs presented great thickening and extensive adhesion of the right pleura, with retraction of the right lung. In one animal small caseous tubercles were found between the layers of connective tissue of the organized exudate. In another a fibro-caseous nodule was found within a vascular granulation in the right parietal pleura; the left lung and other organs were normal. Two of the control guinea pigs showed a fibro-caseous nodule at the point of injection, with local adhesive pleuritis. The right lung of one animal was congested; the right lung of the two other guinea pigs was normal. A few granulations were noted in the liver and spleen of one animal.

[116] The roentgen rays were generated by a Muret tube (40 cm.) operated in connection with a powerful Ruhmkorff coil and Radiguet interrupter which, with an average primary current of 6 amp., gave sparks 45 cm. long. The current was furnished by a battery of 20–30 volts, with a capacity of 80 ampere-hours. Focal-skin distance, 35 to 40 cm.

In a second series of six guinea pigs the animals were inoculated in the same manner, and three of them were exposed to roentgen rays for one hour daily or every second day. Loss of weight again occurred in all the animals. The three exposed guinea pigs died twenty-one, eleven, and ten days, respectively, after inoculation. One of the unirradiated, control guinea pigs was killed twenty-four days after inoculation; one died three days after inoculation (laceration of the lung); through an error in technique the third guinea pig had been inoculated beneath the skin instead of in the pleura. Of the three irradiated animals one presented a caseating lesion in the subcutaneous tissues, and a few granulations in the peritoneum, liver, and spleen (very large).[117] The two others showed great thickening and total adhesive symphysis of the right pleura, with scattered, yellow, tuberculous granulations. In both cases the right lung was markedly retracted and congested. A small tuberculous nodule was found in the left pleura of one animal. Except for a small, encysted tubercle at the level of the second interspace, the first control guinea pig had a normal right pleura and lung and a few granulations in the liver and spleen. The second presented a few loose adhesions around the posterior border of the right lung, a scar with caseating lesions at the point of inoculation, and a large spleen. The third animal died from accidental laceration of the lung.

Twelve other rabbits of about equal weight[118] were inoculated by incising the skin of the neck under aseptic precautions and by injecting, directly into the trachea, two or three drops of a month-old culture of human *Bacillus tuberculosis* in glycerin-bouillon diluted in sterile distilled water. The cutaneous incision was then sutured and covered with a collodion dressing. The rabbits were then divided into two series of six animals. The entire body of three rabbits of one series was exposed to roentgen rays for from ten to sixty minutes daily or every second day; the three other animals were not irradiated, but were kept as controls. The entire body of three rabbits of the other series was exposed to the rays at different intervals after inoculation, and the three other animals were not irradiated but kept as controls. Two days after inoculation, an infection developed in the animals and five of the twelve rabbits succumbed. Of the seven survivors, four were grouped in one series, and three in a second series. Ten days after inoculation, the entire body of two of the rabbits of the first series was exposed to roentgen rays for ten minutes[119] at first and later for one hour (thirty-five days after infection). The two other rabbits of this series were not irradiated, but were kept as controls. The weight of all four animals diminished progressively and about to the same extent. One irradiated rabbit died thirty-nine days, and the other was killed two months and thirteen days, after inoculation. One of the control animals also died thirty-nine days, and the other two months and thirteen days, after inoculation.[120] The trachea of both of the irradiated animals was red and congested throughout, but tubercles could not be found. Tuberculous granulations were found in both lungs of each rabbit; both animals also presented a few granulations in the liver but none in the spleen. Through a technical error, the two control rabbits had been inoculated in the retrotracheal space, where a large, caseating abscess was found. The lungs were normal, but the liver contained a few tubercles. The trachea of the other control rabbit was congested, and the right lung presented a few small tubercles.

The entire body of two rabbits of the second series was exposed to roentgen rays for one hour daily; the remaining animal of this series was kept as a control. One of the irradiated rabbits died fifty-five days, and the other was killed two months and thirteen days, after inoculation. The unirradiated, control animal died fifty-five days after inoculation. The trachea of all three animals was intensely congested. The lungs and liver of both irradiated rabbits contained a few scattered tubercles. The lungs of the control animal showed abun-

[117] This must be regarded as a subcutaneous inoculation.

[118] All the animals received the same food and were kept under identical conditions.

[119] Probably daily or every other day. It is not clear how long such irradiation was continued, but probably until the death of the animals.

[120] Possible error.

dant purulent material in the bronchi, a suppurating, tuberculous infection of the middle lobe and of the upper part of the lower lobe of the right lung, and apical emphysema. A few tubercles were found in the liver. Admitting the small number of animals and technical errors as factors diminishing the value of the experiments, Bergonié and Tessier concluded that roentgen irradiation did not appear to exert a favorable influence on tuberculous lesions and that their results did not encourage the application of roentgen irradiation to human tuberculosis. They drew attention to the extensive and marked pleuritis, and thought this, which they regarded as an effect of the rays on the pleura and lung, was not related to the tuberculous process, since active tubercles were found between the layers of the connective tissue. In view of the fact that the animals had been irradiated before the appearance of the tuberculous lesions, they deduced that irradiation does not prevent infection.

Rudis-Jicinski (1901) inoculated ten guinea pigs and ten rabbits with a culture of *Bacillus tuberculosis* obtained by placing a quantity of sputum in fish bladders filled with veal bouillon containing 2 per cent of peptone and 2 per cent of glycerine; the bladders were then closed, boxed and marked. Stroke cultures on glycerine agar were then prepared from each box and were kept in a brood oven for ten days at 37°C. The preparations, which were agitated once a day, showed under the microscope a thick curled up center, around which threads were wound with bacilli in profusion. Ten days after the animals were inoculated, they were all exposed to roentgen rays daily for some time. Eight animals (6 guinea pigs and 2 rabbits), whose secretions had been rendered alkaline, died of tuberculosis. Others, inoculated from cultures on acid media and irradiated daily for ten seconds, lived and remained apparently well for over two years, when they were killed. At necropsy, six guinea pigs and two rabbits showed caseating pulmonary tuberculosis with cavitation and tuberculous granulations, with marked signs of repair in the upper lobe of each lung. Two animals also had tuberculosis of the brain, one tuberculosis of the liver and one tuberculous enteritis. Among the animals irradiated and killed two years later, 40 per cent showed healed tuberculosis when an acid condition was present,[121] also dense calcification, connective tissue sclerosis and adhesions.

Wohlauer (1909) undertook to test the action of different doses of roentgen rays on the lungs of ten normal guinea pigs of medium size. Two of the animals died spontaneously, and the remainder were killed by a blow to the neck, at varying intervals after irradiation. The entire body of the first animal was exposed to 35X (Kienböck) of roentgen rays[122] in one session of twenty-five minutes, and two days later to 40X (Kienböck)[123] also in twenty-five minutes. The total dose, therefore, was 75X (Kienböck), or seven and one-half times the dose required to induce dermatitis. Clinical disturbances did not manifest themselves until five days after the second irradiation, when the animal became listless and its respiration labored; this lasted for two days, when death occurred. The lungs were hyperemic and studded with punctate hemorrhages. The alveoli were filled with albuminous exudate; the peribronchial and perivascular lymph spaces were widely dilated and contained erythrocytes and leucocytes, including eosinophiles. The thorax only of a second guinea pig was exposed on one day to 8X (Kienböck) of roentgen rays[124] in twenty-five minutes, and the next day to approximately 40X (Kienböck)[125]. The total dose was 48X, or approximately five times the limit of tolerance of the skin. The rest of the body was shielded with lead. The animal died one day after the second exposure of the thorax. The lungs appeared normal, but microscopic examination disclosed hyperemia, slight exudation into the alveolar spaces, normal alveolar

[121] It is not clear whether the acidity refers to acid secretions of the animal or acid media in the cultures used for inoculation.

[122] Rays generated by a Bauer tube with a quality of 7.7 Wehnelt, at a potential of 50 volts, with 6 amperes of primary current and a secondary current of 1.5 ma. at a focal-skin distance of 12 cm.

[123] Bauer tube—quality, 8 Wehnelt; potential, 50 volts; primary current, 5 amp.; secondary current, 0.5 ma.

[124] Bauer tube—quality, 8.5 Wehnelt; potential, 50 volts; primary current, 5 amp.; secondary current, 0.3 ma.; focal-skin distance, 22 cm.

[125] Bauer tube—quality, 7.5 Wehnelt; potential, 50 volts; primary current, 10 amp.; secondary current, 1 ma.; focal-skin distance, 10 cm.

epithelium, and dilatation of the perivascular and peribronchial lymph spaces. The thorax only of a third guinea pig was exposed on one day to 16X[126] in fifteen minutes, but no effect was perceived within one month, when the thorax was again exposed to 45X[127] in thirty minutes. The animal gave no evidence of injury and was killed eleven days after the second irradiation. The lungs appeared normal, except that the vessels and capillaries were hyperemic and the lymph nodes enlarged.

The thorax only of a fourth guinea pig was exposed at one session to approximately 6X[128] in sixteen minutes. The animal behaved normally for nearly two months, when it was killed. The lungs were studded with black points which, on microscopic inspection, proved to be black pigment giving the reaction characteristic of hemosiderin. The thorax only of a fifth, sixth, and seventh guinea pig was exposed at one session to 8X, 7X, and 5X, respectively, of roentgen rays generated under conditions similar to those used for the fourth animal. All three animals acted normally until killed eight days, five days, and two and one-half months, respectively, after irradiation. The lungs of the fifth guinea pig were studded with tiny foci with a yellow center and red border; these proved to be small adenomas, such as are normally found in guinea pigs. Fresh and old hemorrhages, the latter represented by deposits of hemosiderin, also were observed. The lungs of the sixth animal were hyperemic and presented signs of fresh and old hemorrhages; the alveolar epithelium was filled with blood pigment, and the lymph nodes were abnormally large. The lungs of the seventh animal appeared normal, but microscopic examination revealed foci of epithelial proliferation surrounded by strands of connective tissue in the region of the larger bronchi, and dilatation of the perivascular lymph spaces. The entire body of an eighth, ninth, and tenth guinea pig was exposed, in one session of thirty minutes, to approximately 16X of roentgen rays generated under conditions closely resembling those for the fourth animal. They were killed seven, and sixteen days, respectively, after irradiation. Hyperemia was the only abnormality noted in the lungs of the eighth guinea pig; those of the ninth animal showed hyperemia, dilatation of the perivascular lymph spaces, patches of atelectasis, and swollen lymph nodes. The only alteration in the lungs of the tenth guinea pig consisted of large, red foci caused by aspiration of blood from the nose while the animal was being killed.

The death of the two first animals was regarded as due to the excessive irradiation to which they had been subjected, partly as an expression of injury to the body as a whole, and partly as agonal changes. The pulmonary hyperemia found in all but one of the animals and the recent and old hemorrhages noted in several animals were considered as effects of irradiation. The common dilatation of the peribronchial and perivascular lymph spaces was related to congestion. The integrity of the alveolar epithelium was thought to indicate that these cells are "extremely refractory to roentgen rays."

KÜPFERLE (1913), in collaboration with Bacmeister, undertook to study the effect of roentgen rays on tuberculous lesions induced by injecting a culture of human *Bacillus tuberculosis* into the ear vein of an unspecified number of rabbits. Some of the animals were exposed, immediately after inoculation and at intervals of from three to eight days, to small doses of roentgen rays; others were not exposed until four weeks after inoculation, and at intervals thereafter. Control animals, killed four weeks after inoculation, showed diffuse pulmonary tuberculosis. Beginning four weeks after inoculation, the right, left, anterior and posterior aspects of the thorax of one rabbit were exposed to 28X,[129] 30X, 27X, and 24.5X, respectively, of roentgen rays[130] filtered through 3 mm. of aluminium in about twelve weeks, at the

[126] Bauer tube—quality, 9 Wehnelt; potential, 50 volts; primary current, 11 amp.; secondary current, 1 ma.; focal-skin distance, 12 cm.

[127] Bauer tube—quality, 6.5–7 Wehnelt; potential, 50 volts; primary current, 11 amp.; secondary current, 1 ma.; focal-skin distance, 10 cm.

[128] Bauer tube—quality, 7 Wehnelt; potential, 50 volts; primary current, 5 amp.; secondary current, 0.3 ma.; focal-skin distance, 16 cm.

[129] Kienböck units.

[130] Quality of rays, 6–8 Benoist; voltage, not specified; focal-skin distance, 28 cm.

rate of about 2X to 5X every three to eight days. The pulmonary tuberculous lesions in rabbits exposed, immediately or four weeks after inoculation, to such small doses were essentially the same as those found in the control animals. Beginning four weeks after inoculation, the right, left, anterior and posterior aspects of the thorax of a second rabbit were exposed to 93X, 79X, 89X, and 91X, respectively, of roentgen rays[131] filtered through 3 mm. of aluminium. Beginning four weeks after inoculation, the right, left, anterior and posterior aspects of the thorax of a third rabbit were exposed to 81X, 75X, 93.5X, and 75X, respectively, of roentgen rays,[131] filtered through 3 mm. of aluminium.

On microscopic examination, twelve weeks after inoculation and eight weeks after the first exposure to roentgen rays, the extensive tuberculous lesions in the lungs of irradiated and unirradiated rabbits differed considerably. In the lungs of the irradiated animals the tuberculous granulations had been replaced by hyaline connective tissue to a surprising extent; this change was most pronounced at the periphery of the tubercles. In the lungs of unirradiated animals the tuberculous process was characterized by active proliferation of tuberculous granulation tissue, and proliferation of connective tissue was not a prominent feature. The active proliferation of connective tissue and the tendency of the irradiated pulmonary tubercles to encapsulation was attributed to the action of the rays, and Küpferle concluded that hematogenous pulmonary tuberculosis can be affected by roentgen rays.

Manoukhine (1913) injected one milligram of a culture of *Bacillus tuberculosis* under the skin of the right side of the abdomen of each of two *Macacus cynomolgus* monkeys (first group) and of four other *Macacus cynomolgus* monkeys (second group), and 0.1 milligram of the same culture was injected subcutaneously (same region) into each of four *Macacus rhesus* monkeys (third group). Five of the animals were kept as controls. The splenic region of the five other monkeys was exposed to about 1 H[132] of roentgen rays filtered through 1 mm. of aluminium; in one animal of the first group irradiation was not started until one week after inoculation, and was repeated every five or six days during the first five weeks, then every three or four days.[133] In the two monkeys of the second group, irradiation was interrupted for two and a half weeks after the three first exposures; then one monkey was irradiated every two to four days and the other every four to eight days. The two animals of the third group were irradiated every two or three days. The control monkey of the first group died thirty-seven days after infection, the two controls of the second group died forty-five and forty-seven days, respectively, after infection, and the two controls of the third group died thirty-seven and thirty-nine days, respectively, after infection. All five animals presented tuberculous granulations at the site of inoculation and, at necropsy, pronounced evidences of generalized tuberculosis were found in the peritoneum and omentum, but especially in the liver, spleen and lungs, which were filled with tuberculous foci.

Of the five monkeys exposed to roentgen rays only one from the second group, whose spleen had been irradiated at rather long intervals, died a natural death, seventy-seven days after infection. In the irradiated monkey of the first group, which was killed eighty days after infection, the tuberculous lesions in the liver and spleen were less numerous and smaller than those in the corresponding organs of the control animals; the lungs were free from such lesions. In the second monkey of the second group, killed ninety days after infection, the point of inoculation was not surrounded by tuberculous granulations; during the two and a half weeks during which the exposures were interrupted, a swelling developed at this point and persisted for sixty-three days. At necropsy, the spleen was normal in size, and it and the liver contained only a few tuberculous foci; such lesions were not found in the lungs. One animal of the third group was killed thirty-nine days after infection; one of the controls died on the same day. Only three tuberculous foci were found in the lungs; the spleen and liver were

[131] Quality of rays, 8–10 Benoist; voltage, not specified; focal-skin distance, 25–28 cm.
[132] Holzknecht radiochromometric units.
[133] Manoukhine did not describe the mode of irradiation or specify how long such periodic irradiation was continued.

normal. The other animals of the same group, killed fifty-eight days after infection, showed a healed abscess at the site of inoculation and slight involvement of the lungs, but the other organs were normal. Thus, all the irradiated monkeys outlived the control animals, and in four of the five exposed monkeys the tuberculous lesions in the internal organs were less extensive than corresponding lesions in the control animals.

In twenty guinea pigs 0.01 milligram of a culture of *Bacillus tuberculosis* was injected subcutaneously; ten animals were irradiated[134] two days after infection and every two to four days thereafter. Four of the ten control animals died from accidental infection. In six guinea pigs that died from seventy to ninety-three days after infection the spleen was from five to ten times larger than normal; in one animal the organ was twenty or twenty-five times larger than the normal spleen. Tuberculous foci were found in the spleen, liver and lungs. Four irradiated guinea pigs died from accidental infection. The six other animals were killed on the day the last control animal succumbed. In two the size of the spleen was normal; in the four others the spleen was one and a half times or twice the size of the normal organ, and in three animals the spleen contained tuberculous granulations, while the other organs appeared normal. In two animals, irradiation seemed to have prevented tuberculous infection; in the others only slight tuberculous changes were noted.

Küpferle and Bacmeister (1913) attempted to determine, in adult rabbits, the effect of roentgen rays on pulmonary tuberculosis induced experimentally by injecting into the vein of the ear uniform doses of tubercle bacilli of human type or by causing the rabbits to inhale dust laden with such bacilli. Some of the animals inoculated through the ear were exposed, immediately afterward, to from 2 to 5[135]X of roentgen rays,[136] and this was repeated at intervals of from three to eight days. During the successive irradiations the animals were immobilized and the localizing cone was centered successively over the back, thorax, right and left sides.[137] The total irradiation time was from eleven to thirteen hours within a period of twelve weeks. The total surface energy was 109.5X, and the ratio of energy at the proximal and distal surfaces was 3.6:1.0. Thus, one-fourth of the roentgen energy passed through unabsorbed. Microscopic inspection of the lungs of rabbits irradiated in this manner failed to disclose any influence on the tuberculous process.

A second series of rabbits, which had already been irradiated by the foregoing method, was then exposed daily or every other day for from thirty-five to forty minutes, to from 15 to 25X of high-voltage roentgen rays.[138] Irradiation was not started until four weeks after inoculation. The total surface dose given to some of the animals was between 325X and 352X in fifteen or sixteen hours, spread over a period of about eight weeks; several unirradiated rabbits were kept as controls. The control animals, killed three and one-half months after inoculation, presented many large, protuberant, coalescing and caseating tubercles throughout the pleura and lungs, and microscopic examination confirmed the macroscopic impression. The pleura adjacent to the tubercles was thickened and infiltrated with cells; the center of the tubercles, which sometimes gave evidence of beginning calcification, was surrounded by a dense wall of inflammatory granulation tissue. The alveoli adjoining the tuberculous lesions exhibited pneumonic infiltration, and this extended along the vessels and bronchi. In the lungs of the irradiated rabbits, which were likewise killed three and one-third months after inoculation, numerous tubercles appeared in the pleura, but their evolution was less advanced, and they were more sharply delimited from the neighboring normal lung sub-

[134] Same dose as for the monkeys.

[135] Kienböck units.

[136] The rays were generated by a simple "inductor" with mercury interrupter; they were filtered through 3 mm. of aluminium; the focal-skin distance was 28 or 30 cm.; the quality of the rays was given as 6 to 8 Benoist, but the voltage was not specified. Such rays would now be regarded as of relatively long wave-length.

[137] Presumably over the four aspects of the thorax. The size of each field was not given.

[138] The rays, filtered through 3 mm. of aluminium, were generated in Müller tubes by a Veifa Reform high tension, alternating current generator, with tube rectification. The focal-skin distance was reduced to 20 and 22 cm. The quality of the rays was given as between 8 and 10 Benoist. Such radiation would now be regarded as of medium quality.

stance; central caseation was less marked, young connective tissue surrounded and penetrated the degenerating center of the tubercles, and the surrounding zone of pneumonic inflammation was generally lacking.

These effects of irradiation were investigated further by exposing a third series of rabbits,[139] beginning one day after inoculation, to daily surface doses of from 10X to 35X under the same conditions as for the second series. The irradiation period extended from two and a half to four and a half weeks. The lungs of a control animal, inoculated at the same time and killed two and two-thirds months later, revealed innumerable subpleural and pulmonary tubercles, with beginning central caseation or extensive necrosis and marked inflammatory reaction. Two of the irradiated rabbits died nineteen and twenty-two days, respectively, after inoculation. The lungs of these animals showed only a few indefinite, gray, subpleural nodules, and microscopic inspection disclosed only occasional small foci, which were not typical tubercles but consisted largely of connective tissue. Two other rabbits, which had been irradiated in much the same way, and an unirradiated control animal were killed thirty-three days after inoculation. Again, a great difference between the control and irradiated rabbits was found. The only evidence of tuberculosis in the lungs of the latter consisted in small, fibrous foci, without caseation.

Küpferle and Bacmeister concluded that irradiation acts chiefly on the early, infiltrative stage of the tubercles and hinders the evolution of the lesions; that it also affects the more advanced tubercles to a smaller degree, and that large total doses are necessary to influence the tuberculous process; but they were unable to demonstrate a direct action on the bacilli themselves.

Küpferle (1914) sought to determine the influence of roentgen rays on the incidence and course of tuberculous infection of the lung, their action on the infecting bacteria or on the tissue cells, and the effect of variation in quality or quantity of the rays. *Bacillus tuberculosis* was injected into the ear vein of rabbits,[139] some of which were at once exposed to a small dose of rays of medium quality; during a period of three months the right, left, posterior and anterior aspects of the thorax received a total surface dose of 110X (Kienböck)[140] in a total irradiation time of approximately eleven hours. This did not have any perceptible effect on the pulmonary tuberculous process; the lesions in the exposed rabbits and in the unexposed, control animals were essentially the same. A second series of rabbits,[141] infected in the same manner, was exposed to large doses immediately after inoculation and almost daily thereafter for from two and a half to four and a half weeks.[142] During this period, some of the animals received a total surface dose of 396X in a total irradiation time of eleven hours, while others received a total surface dose of 509X in a total irradiation time of approximately sixteen hours. Details of irradiation and pathologic findings in only two rabbits were given as examples.

In one animal (396X) only fine foci of tuberculosis, largely made up of connective tissue, were scattered through the lungs; the same was true of the other animal (509X), in which the lesions were even more fibrous; evidence of necrosis or active inflammation could not be found. In the unirradiated, control animals, on the contrary, typical tubercles with central caseation could be seen with the naked eye, and the lesions showed a distinct tendency to progression and tissue destruction.

Several rabbits with fully-developed pulmonary tuberculosis, that had previously been exposed to small doses of rays, later were subjected to large doses of hard[143] rays daily for

[139] Number not stated.

[140] This qualification would no longer apply; such rays would now be regarded as of medium quality. Rays of short wavelength were not obtainable at that time.

[141] Number not mentioned.

[142] A surface dose of 20 X–30 X, in from 30 to 40 minutes at each session, was given successively to the right, left, posterior and anterior aspects of the thorax. The rays were filtered through 3 mm. of aluminium, and the focal-skin distance was 18–20 cm.

[143] This qualification would no longer apply; such rays would now be regarded as of medium quality. Rays of short wave length were not obtainable at that time.

about five weeks. The irradiated and unirradiated animals were killed at the same time, twelve weeks after the first exposure.[144]

The appearance of the lungs in the exposed and unexposed rabbits differed greatly. Whereas the lungs of the control animals showed large and small tubercles undergoing caseation, surrounded by granulation tissue, with a tendency to extend into adjacent normal lung tissue by proliferation, the character of the tuberculous process in the lungs of irradiated rabbits was quite different. Necrosis was a much less prominent, and calcification a much more prominent, feature. Granulation tissue, so prevalent around the tubercles in unirradiated lungs, was replaced, in lungs that had been exposed to the rays, by a broad band of connective tissue around the necrotic, central portion of the tubercle. The rays had destroyed the granulation tissue and increased the proliferation of connective tissue. Moreover, the effectiveness of the rays was related to their quantity rather than to their quality. An effect on the bacilli themselves could not be demonstrated by transplantation experiments.

Küpferle and Bacmeister (1916) continued their investigations of the action of roentgen rays on pulmonary tuberculosis, induced experimentally in rabbits by hematogenous inoculation and by inhalation of bacteria-laden dust. Their object was not only to ascertain further the effect of irradiation on tuberculous lesions, but also to determine the technique of irradiation most effective against such lesions. Four rabbits, inoculated through the vein of the ear, were exposed, immediately afterward and again at intervals of from three to nine days for varying periods, to doses of from 15X to 17X[145] of roentgen rays;[146] the total dose varied from 185X to 390X. Microscopic examination of the lungs of the first and third animals, which had received total doses of 185X and 307X, respectively, showed numerous tubercles with more or less central caseation, surrounded by a zone of cellular infiltration and granulation tissue, and with scattered areas of pneumonia, but the appearance of the tubercles did not differ appreciably from that of tubercles in the control rabbits. The tubercles in the second rabbit, which had received a total dose of 389X, showed a slightly less extensive zone of inflammatory reaction, but the difference between this rabbit and the control animals was slight. In the fourth animal, which had received a total dose of 390X, however, the tubercles were smaller, exhibited less central caseation and surrounding cellular infiltration, and the connective tissue about them was studded with larger calcareous foci than were corresponding lesions in the control animals.

Three other rabbits, likewise inoculated through the blood stream, were not exposed to roentgen rays until four weeks after infection and then received, at intervals of from three to seven days over a period of less than three months, average doses of from 20.9X to 23.2X, or total doses of 374X, 405X, and 397X, respectively, in a total irradiation time of from eleven and one-half to eleven and three-fourths hours. The lungs of the control animals, inoculated at the same time and in the same manner but not irradiated, presented numerous subpleural tubercles, some of which were as large as beans and all of which showed a broad zone of reactive inflammation around relatively small, caseated centers, with marginal hyperemia, scattered areas of pneumonia, and perivascular and peribronchial infiltration. The lungs of the irradiated rabbits showed fewer and smaller tubercles, caseation was either absent or slight, and the lesions were undergoing perceptible sclerosis. The foregoing macroscopic features were confirmed by microscopic inspection. Whereas the lungs of the unirradiated control animals gave the picture of florid tuberculosis, with numerous coalescing lesions, extensive caseation, and sometimes cavity formation, those of the irradiated rabbits showed much less extensive caseation or no caseation at all, rather dense young connective tissue, little if any specific granulation tissue, and active calcification; in other words, rapidly

[144] Details of irradiation and pathologic findings in only one rabbit were given as an example.

[145] Kienböck units.

[146] The technical factors of irradiation presumably were the same as in their earlier experiments, but no mention of such factors was included in the report.

advancing organization and repair. Lung tissue from all of the irradiated animals was injected into guinea pigs, and all contracted tuberculosis; thus proving that roentgen rays may influence the lesions of tuberculosis without destroying the bacilli.

In a third series of five rabbits, inoculated intravenously, the animals were not exposed to roentgen rays until six weeks after infection, and then received daily or at intervals of one or two days, for periods varying between sixteen and forty-two days, average doses of from 22.2X to 30.5X, or total doses of 1037X, 605X, 676X, 379X and 346X, respectively. The lungs of the control animals showed lesions such as those which characterize tuberculous infection through the blood stream. The lungs of the irradiated animals, on the contrary, did not give evidence of florid tuberculosis; the salient feature of the lesions was proliferation of connective tissue, in which appeared small areas of necrosis and calcification. In the lungs of all but one of the rabbits were found extensive, acute bronchitic and pneumonic manifestations which had brought two of the animals to death. These pneumonic changes were especially great in the rabbit that had received the strongest dose of radiation within six weeks. The single animal that did not present bronchitic and pneumonic disturbances was that which had received the smallest dose (346X). Küpferle and Bacmeister deduced that irradiation had inhibited the evolution and favored the healing of the tuberculous lesions, but that such strong doses of roentgen energy in a short time probably had caused the severe bronchitis and bronchopneumonia.

Similar experiments were carried out on rabbits, in which tuberculosis of the lungs was induced by causing the animals to inhale bacilli-bearing dust. A description of these studies was not given, the authors merely stating that the results were the same as those obtained in animals inoculated intravenously. Small doses of roentgen rays, distributed over a long period of time, had no effect; but larger doses, repeated more frequently, inhibited the evolution of tubercles and caused them to heal more rapidly; excessive doses caused pulmonary irritation leading to bronchitis and bronchopneumonia.

Schröder (1921), on the basis that the rabbit possesses a rather high natural resistance to the human type of *Bacillus tuberculosis*, criticized the earlier experiments of Küpferle and Bacmeister and undertook to repeat them. He selected a series of rabbits of the same weight, from the same litter, and, in order to provide comparable conditions, injected a small dose of the bovine type of *Bacillus tuberculosis* subcutaneously into some animals and intravenously into others. The rabbits, divided into groups of two, were then exposed to small, moderate, or large doses of roentgen rays.[147] In each case an additional group of two rabbits was used for control purposes.

Two rabbits received, subcutaneously, 0.1 mg. of the *B. tuberculosis* culture, and two rabbits received 0.05 mg. intravenously. In animals injected subcutaneously, the point of injection, later the infected lymph nodes, and later still the lungs, were irradiated. In animals injected intravenously, the left and right halves of the thorax were exposed alternately to one-third of the human skin unit dose one week after injection and at intervals of one week thereafter. Thus, the rabbits of the first group received a total dose of 72X (Kienböck); in the second group, one rabbit received 18X and the other 36X. The animals in which the organism was injected subcutaneously survived longer (125 to 135 days) than the control animals (87, 103 days), while those in which the organism was injected intravenously died sooner than the controls (19 and 51 days against 90 and 32 days, respectively). In the former also, the irradiated animals lost more in weight than the non-irradiated rabbits. To the naked eye the tuberculous lesions in the irradiated and unirradiated rabbits did not appear to differ. In the latter, however, the infected lymph nodes were larger than in the former.

[147] The rays were generated by means of a Müller boiling-water tube, with osmo-distant regulation, electrically supplied by an Apex generator (Reiniger, Gebbert and Schall), with gas motor interrupter. The hardness of the tube was rated as 10 of the Bauer scale; the potential was equivalent to a parallel spark-gap of 25 cm.; current, 2.5 ma.; filtration, 3 mm. of aluminium; focal-skin distance, 23 cm.; size of field, 26 square cm. Dose, 25 × (Kienböck) or 1 H.E.D.

Two other rabbits of the same weight, from the same litter, received, subcutaneously, 0.1 mg. of the same strain of *Bacillus tuberculosis*, and the point of infection was exposed to one human skin unit dose of roentgen rays one week after inoculation and at intervals of eight days thereafter (total for both animals, 117X). The irradiated animals survived as long as the controls (95 and 95 days against 115 and 91 days, respectively), and loss of weight in the former was less than in the latter. At necropsy, the tuberculous lesions were similar to those found in the first series of rabbits. In animals infected through the skin, histologic examination of the axillary nodes on the infected side disclosed that evolution of the tuberculous process was less advanced in the irradiated than in the unirradiated animals. In the former, some of the nodes had become transformed into connective tissue, while other nodes showed a sharp line of demarcation between the caseated center and the thickened capsule. In the control rabbits the nodes were larger, entirely caseated, and did not present evidence of connective tissue repair. As for the internal organs, the tuberculous lesions in the irradiated and unirradiated rabbits did not differ appreciably. In animals infected through the blood stream, the lesions in the irradiated and unirradiated animals did not show the slightest difference.

In another series of eight rabbits of the same weight, from the same litter, only 0.05 mg. of culture was injected subcutaneously. In two rabbits irradiation was started one week, in two two weeks, and in two four weeks, after injection; the two remaining rabbits were left unirradiated to serve as controls. Of each of the three irradiated groups one animal was exposed to one skin unit dose and the other to 0.6 of the skin unit dose.[148] One rabbit of the first pair received altogether 313X and survived eighty-three days, and the other rabbit received 150X and survived one hundred and twenty days. One rabbit of the second pair received altogether 205X and survived ninety days, while the other rabbit received 100X and survived fifty-five days. One rabbit of the third pair received altogether 175X and survived one hundred and three days, while the other rabbit received 90X and survived seventy-three days. The unirradiated, control animals survived ninety-nine and eighty days, respectively. The irradiated rabbits lost between 600 gm. and 900 gm., while the two control animals lost 400 gm. and 1,150 gm., respectively. The tuberculous lesions in the irradiated and unirradiated animals were approximately the same and consisted in small, partly caseating nodules in the lungs, mediastinal nodes, kidneys, liver, and intestine. In the rabbits exposed to the larger dose of rays, the point of infection was healed by a scar, and only small hard nodes with a thickened capsule were found; in the rabbits exposed to the smaller dose, the point of infection still showed flat tuberculous infiltration, part of which had undergone caseation. In the control animals, on the contrary, large groups of infected subcutaneous nodes surrounded the site of primary infection. A definite influence of the rays on body weight or duration of life could not be established.

On microscopic examination, the tuberculous lesions in the irradiated rabbits were fewer and smaller than in the unirradiated, control rabbits. For example, the tuberculous foci in the kidneys of the control animals were extensive and actively undergoing caseation, while those in the kidneys of irradiated animals usually appeared as solitary tubercles; such difference was not found in the lungs. Schröder summarized his results by stating that roentgen rays did not influence tuberculous lesions in the lungs, but did have an unmistakably beneficial effect on lesions around the point of inoculation and on tuberculous lymphadenitis; also, that one skin unit dose was more effective than smaller doses.

Gorke and Töppich (1922), having found that in only four of fourteen rabbits, inoculated with tuberculosis and treated with Krysolgan, did the tuberculous lesions differ from corresponding lesions in control rabbits and that, in the majority of the inoculated animals, the use of this preparation had not had any apparent effect, undertook to determine the combined influence of Krysolgan and roentgen rays. They assumed that small or so-called stimu-

[148] Presumably human skin unit dose.

lating doses of roentgen rays are most effective against pulmonary tuberculosis. They first inoculated eleven rabbits with *Bacillus tuberculosis;* one of the animals was left untreated to serve as control, while the ten other rabbits were exposed to roentgen rays and also were treated with Krysolgan. To provide a still better basis of comparison, only one lung of each of the ten animals was irradiated; in this way the irradiated lung could be compared, not only with the lungs of the unirradiated rabbit but also with the unirradiated lung of the same animal. The ten rabbits were divided into three groups: four in the first group, and three in each of the two other groups. The anterior and posterior aspects of one-half of the thorax of each animal were irradiated[149] alternately at intervals of from three to five days

Series A. The left lung of one rabbit was exposed to roentgen rays twelve times in fifty-eight days, between the one hundred and twenty-fourth and the one hundred and eighty-second days following inoculation, received a total dose of 96X,[150] and the animal was killed seven days after the last irradiation. The miliary tubercles in the exposed left lung and unexposed right lung did not differ perceptibly. The left lung of a second rabbit was exposed to roentgen rays ten times in fifty-five days, between the two hundred and eightieth and the three hundred and thirty-fifth days following inoculation, received a total dose of 80X, and the animal was killed seven days after the last irradiation. The microscopic features of the tuberculous process in the exposed left lung and in the unexposed right lung did not differ. The left lung of a third rabbit was exposed to roentgen rays twelve times in fifty-five days, between the one hundred and twelfth and the one hundred and fortieth days following inoculation, received a total dose of 96X, and the animal was killed thirteen days after the last irradiation. Between the one hundred and twelfth and one hundred and fortieth days of the disease, this animal had also received five injections of Krysolgan.[151] The microscopic features of the tuberculous lesions in the exposed left lung and in the unexposed right lung did not differ appreciably. The left lung of a fourth rabbit was exposed to roentgen rays twelve times in fifty-six days, between the one hundred and sixteenth and one hundred and seventy-second days following inoculation, received a total dose of 96X, and the animal was killed ten days after the last irradiation. Between the one hundred and eighth and one hundred and sixtieth days of the disease, the animal had also received six injections of Krysolgan.[152] The microscopic features of the tuberculous lesions in the exposed left lung and in the unexposed right lung did not differ appreciably.

Series C. The left lung of one rabbit was exposed to roentgen rays twelve times in forty-seven days, between the eighteenth and sixty-fifth days following inoculation, received a total dose of 96X, and the animal was killed forty-three days after the last irradiation. The microscopic features of the tuberculous lesions in the exposed left lung and in the unexposed right lung did not differ appreciably. The left lung of a second rabbit was exposed to roentgen rays eight times in forty days, between the seventh and forty-seventh days following inoculation, received a total dose of 64X, and the animal died four days after the last irradiation. Between the fifteenth and the forty-fifth days of the disease, this animal had also received four injections of Krysolgan.[153] The microscopic features of the tuberculous lesions in the exposed left lung and in the unexposed right lung were essentially the same. The left lung of a third rabbit was exposed to roentgen rays twelve times in fifty-seven days, between the seventeenth and seventy-fourth days following inoculation, received a total dose of 96X, and the animal was killed thirty-four days after the last irradiation. Between the fifteenth and the seventy-third days of the disease, the animal had also received six injections of

[149] The rays were generated by a Müller boiling-water tube supplied by an Apex apparatus with gas-motor interrupter. The hardness of the tube was 6 or 7 of the Walter scale, the intensity of current was 2.2 ma., the rays were filtered through 3 mm. of aluminium, and the focal-skin distance averaged 23 cm.

[150] Kienböck units.

[151] 2, 5, 10, 10, and 10 mg., respectively.

[152] 1, 2, 5, 5, 10, 10, and 10 mg., respectively.

[153] 5, 8, 10, and 12 mg., respectively.

Krysolgan.[154] The microscopic features of the tuberculous lesions in the exposed left lung and in the unexposed right lung were essentially the same.

Series D. The right lung of one rabbit was exposed to roentgen rays twelve times in fifty-four days, between the ninth and the sixty-third days following inoculation, received a total dose of 96X, and the animal was killed twenty-nine days after the last irradiation. The microscopic features of the tuberculous lesions in the exposed right lung and in the unexposed left lung were essentially similar. The right lung of a second rabbit was exposed to roentgen rays twelve times in fifty-four days, between the ninth and sixty-third days following inoculation, received a total dose of 96X, and the animal was killed twenty-nine days after the last irradiation. The microscopic features of the tuberculous lesions in the exposed right lung and in the unexposed left lung did not differ appreciably. The right lung of a third rabbit was exposed to roentgen rays twelve times in fifty-four days, between the ninth and sixty-third days following inoculation, received a total dose of 96X, and the animal was killed twenty-nine days after the last irradiation. This animal had also received six injections of Krysolgan.[155] The microscopic features of the tuberculous lesions in the exposed right lung and in the unexposed left lung did not differ appreciably.

Whether irradiated or treated with Krysolgan, a perceptible difference in the macroscopic or microscopic appearance of the tuberculous lesions in the lungs of these animals could not be found. Gorke and Töppich concluded that the doses of roentgen rays which they used did not affect the course of the tuberculous process.

Warren and Whipple (1922) tested the comparative sensitiveness of the thoracic and abdominal organs to roentgen rays, by exposing the thorax and abdomen of three adult dogs, and later the abdomen only of two of these dogs, to from 350 to 450 milliampere-minutes of rays of medium wave-length. A more detailed description of these experiments will be found elsewhere.[156] Severe clinical disturbances, including diarrhea, vomiting and prostration, and marked pathologic changes featured by extensive degeneration, hemorrhagic extravasation, edema, and desquamation of the epithelium and mucosa of the small intestine, atrophy of the spleen, degenerative changes in the ovary, and moderate destruction of lymphocytes in the lymph nodes, intestinal follicles, and bone marrow, were noted in all the animals after irradiation of the abdomen. But, except for transient leucopenia and a slight rise in urinary nitrogen, neither clinical manifestations nor pathologic alterations in the lungs or heart were found in any of the animals after irradiation of the thorax.

Swann (1924) sought to determine the immediate, functional effect of roentgen rays on various organs by exposing usually the entire body of an unspecified number of cats, guinea pigs, and rabbits to unfiltered rays of medium quality[157] for different periods. A marked and progressive fall in blood pressure was noted after three or four fifteen-minute exposures of the thorax and abdomen, broken by short intervals of rest. Some of the animals died after the second exposure; death was never due to respiratory failure, because life could not be prolonged by artificial respiration, which continued after the heart had ceased to beat, but always to cardiac failure. Respiration increased in depth and frequency at first, but later marked respiratory depression occurred. Swann found that stronger and stronger faradic currents were required to produce the same initial increase in respiration. Other experiments, a description of which is given elsewhere (page 4), were conducted on the isolated heart of frogs and rabbits. The important results were that prolonged irradiation caused the tone of the cardiac muscle to increase progressively until the heart ceased to beat in systole,

[154] 5, 8, 10, 12, 15, and 20 mg., respectively.

[155] 5, 7, 9, 10, 12, and 12 mg., respectively.

[156] See Action of Roentgen Rays and Radium on the Gastrointestinal Tract. Am. J. Roentgenol. & Rad. Therapy, 1931, *26*, 145, 335, 493.

[157] The rays were generated by gas tubes of the same make, operated at a potential equivalent to a point-plate spark-gap of from 4 to 7 inches; the focal-skin distance varied between 6 and 10 inches; and the intensity of the current, between 1 and 2 milliamperes.

and this was accompanied by constriction of the bronchial muscles, tonic contraction of the uterus, and increase in tone of the intestine.

Davis (1924) undertook to investigate, in an unstated number of rabbits and dogs,[158] the action of roentgen rays on the normal lung and the character of such action. The animals were carefully selected, and the controls were kept in the same surroundings as the experimental subjects. Sufficient time was allowed before the experiments to exclude distemper. The blood and urine were not examined, but a clinical record of respiratory symptoms, loss of weight, and other disturbances was kept. From 0.016 to 0.032 gm. of morphine was used to keep the dogs quiet during irradiation. In some of the experiments, the entire thorax was exposed to the rays, and other animals were used as controls. In most of the experiments, however, only the right half of the thorax was irradiated, and the left lung of the same animal served as control. The dose of roentgen rays at each exposure and the number and time of such exposures were not given for all the animals. Such complete data were furnished for only two rabbits and one dog, but the changes observed in these three animals were described as representative of all the animals. In all the animals, the dose of roentgen rays was sufficient to induce a permanent alopecia corresponding to the field of irradiation; a third degree radiodermatitis occurred in but one animal. The skin of the animals was found more resistant to roentgen rays than that of human beings.

Two healthy, normally active rabbits were isolated and kept on the same diet and under the same living conditions. One of these animals, for which complete data were furnished, was irradiated[159] five times at intervals of twenty, seven, thirty, and one hundred and four days, respectively: four times through a right anterior thoracic field 3x3 cm., and once through a right posterior thoracic field 3x4 cm., with the rest of the body shielded by lead 2 mm. thick. The unexposed control rabbit remained well throughout. Except for a slight, transient loss of weight following each exposure and apparently related to the anorexia incidental to irradiation, the irradiated animal also remained well until one week after the last exposure, when dyspnea developed, the animal refused to eat, and its weight fell rapidly. It was killed with chloroform, two weeks after the last irradiation. At necropsy, two areas of alopecia corresponded to the irradiated regions of the right anterior and posterior aspects of the thorax. The peritoneum, stomach, and intestine were normal in appearance. The right pleural cavity contained 25 c.c. of fluid, and the parietal and visceral layers of the pleura adhered at many points. The pericardium also contained an abnormal quantity of fluid and presented fibrinous adhesions. The left lung was normal in appearance, consistency and crepitation. On the contrary, the density of the right lung, especially of the middle lobe which had shrunk to about one-fifth of its normal size, was greatly increased, and on section, the normal markings were obscured. Microscopic inspection showed marked thickening of the alveolar walls, with reduction in size or obliteration of the air spaces, normal alveolar epithelium, increase in the connective tissue surrounding the bronchi and blood vessels, and great thickening of the blood vessels (especially the media) in the affected area. These abnormalities were most marked in the middle lobe, in which no air-containing structures remained. The unirradiated left lung was normal. Pulmonary abnormalities of the same character were found in all the other rabbits subjected to thoracic irradiation, but none of these presented evidence of pleural or pericardial reaction.

Another rabbit was exposed to roentgen rays[160] twice, with an interval of twenty-three days, through a circular field 1.25 centimeters in diameter, over the anterior aspect of the

[158] Twelve or more.

[159] Universal Coolidge tube operated in connection with a Kelley-Koett oil-immersed transformer, with mechanical rectifier, at a potential of 85 peak kilovolts (sphere-gap), at a focal-skin distance of 25 cm., with 5 ma. of current, and 2 mm. of aluminium filtration. The time of exposure on four occasions was 28 min., and on the fifth occasion, 30 min.

[160] Universal Coolidge tube operated in connection with a Kelley-Koett oil-immersed transformer, with mechanical rectifier, at a potential of 135 peak kilovolts (sphere-gap), at a focal-skin distance of 20 cm., with 5 ma. of current and 4 mm. of aluminium filtration. The duration of the first exposure was 30 minutes, and of the second, 60 minutes.

right half of the thorax. The first irradiation had no apparent effect, but seven days after the second exposure, the animal became dull and weak, lost rapidly in weight, developed marked dyspnea and fever, and was killed with chloroform, eleven days after the second session of irradiation. Emaciation, inflammatory infiltration, alveolar edema, epithelial desquamation, and interalveolar hyperemia of the lower lobe of the right lung were the only pathologic changes found at necropsy. Similar alterations were noted in the animals irradiated excessively, in which acute symptoms occurred. The right anterior aspect of the thorax of a normal dog was exposed to roentgen rays[161] four times, at intervals of fourteen, twenty-two, and twenty days, respectively. Except for a transient loss of weight following each irradiation and slight dyspnea during the last few weeks of life, the animal remained in good health throughout; it was killed with chloroform fifty-four days after the last exposure. At necropsy, two areas of alopecia corresponded to the areas exposed to the rays. The peritoneum, intestinal mucosa, and pleural cavity appeared normal. An area of reddish-blue discoloration in the upper lobe of the right lung corresponded to the field of irradiation; the lungs were otherwise normal. When inflated, all the lobes of both lungs expanded normally, except the affected area in the right upper lobe, which offered resistance to the knife. The anterior wall of the right auricle of the heart was greatly thickened, and numerous petechial hemorrhages dotted the pericardium. Microscopic inspection corroborated the macroscopic appearances. The affected portion of the upper lobe of the right lung exhibited marked thickening of the alveolar walls and consequent reduction in size of the air spaces, with occasional desquamation of the lining epithelium, thickening of the blood vessels and increase in the perivascular and peribronchial connective tissue, marked increase of the connective tissue in the subserous areolar tissue of the pleura, areas of necrosis in the wall of the right auricle of the heart, with hemorrhagic extravasation, necrosis and hyalinization of some of the cardiac muscle fibers, and proliferation of connective tissue in the necrotic areas and around the blood vessels. Similar changes were found in all but two of the dogs. Davis concluded that excessive irradiation of the thorax may induce more or less severe inflammation of the lungs and pleura, and that such changes may lead to fibrosis and impairment of respiratory function.

Tsuzuki (1926) exposed the entire body of rabbits to roentgen rays of short wave-length. A more detailed description of his experiments is given elsewhere.[162] In one series of experiments, twenty-nine rabbits received from 20 to 100 per cent of the human erythema dose at one sitting, and the effect was observed over a period of fifty-six days. All the internal organs were subjected to macroscopic and microscopic inspection. A single irradiation of over 40 per cent of the human erythema dose resulted in death sooner or later. More or less extensive pathologic alterations were found in many organs including the liver, kidneys, and bone marrow, but the earliest and most pronounced effects were on the different elements of the lymphatic system and on the genital glands. These degenerative changes are described in the sections dealing with these various organs and structures. As far as the lungs were concerned, strong irradiation caused hyperemia, edema, and serous exudation, but these diminished rapidly and were followed by an increase in the pigment cells. "In the lungs of the animals which died in an exhausted condition, a congestion resembling pneumonia was often observed."

In a second series of experiments, twenty-three rabbits received from 10 to 80 per cent of the human erythema dose in from 15 to 120 minutes, and were killed at intervals of from 15

[161] Universal Coolidge tube operated in connection with a Kelley-Koett oil-immersed transformer, with mechanical rectifier, at a potential of 135 peak kilovolts (sphere-gap), at a focal-skin distance of 12 cm., with 5 ma. of current and 6 mm. of aluminium filtration. The duration of the first, second, and fourth exposures was 60 minutes; and of the third, 30 minutes. Field of irradiation, 8 ×8 cm.

[162] See Action of Roentgen Rays and Radium on the Gastrointestinal Tract. Am. J. Roentgenol. & Rad. Therapy, 1931, *26*, 145, 335, 493.

minutes to 96 hours after irradiation. Again, as in the first series, destructive or degenerative cellular alterations were found in many organs. The changes in the lungs were featured by degeneration or destruction of the nuclei of lymphocytes in the peribronchial tissues, infiltration of pseudo-eosinophile cells, and hyperemia. The degree of these abnormalities varied with the dose, and they were later replaced by a gradual increase in the pigment cells. After still larger doses of roentgen rays, the alveolar and bronchial epithelium desquamated, and this was accompanied by hyperemia, serous exudation in the alveoli, and by phagocytosis of chromatin granules. These abnormalities disappeared after thirty-six hours. After extreme doses, the pulmonary changes were more severe and varied from hyperemia and edema to exudative and hemorrhagic alveolitis and bronchitis; but even these alterations disappeared after twenty-four or thirty-six hours.

In a third series of experiments, six rabbits were exposed to roentgen rays continuously until they died. Two succumbed after 180 minutes of irradiation (120 per cent of the human erythema dose); one after 200 minutes (130 per cent of the human erythema dose), and one after 220 minutes (150 per cent of the human erythema dose). The two remaining animals were irradiated for 240 minutes; one died one hour, and the other two hours, afterward. As the irradiation progressed, the animals became weaker and weaker and died in an exhausted condition, with hemorrhagic frothing from the mouth and tonic spasms of the extremities. The salient pathologic changes were: marked hyperemia of most of the organs; extensive destruction of lymphocytes in the spleen, mesenteric lymph nodes, intestinal lymph follicles, bone marrow, and thymus; degenerative changes in the testis, kidney, salivary glands, and liver; and fatty degeneration of the cardiac muscle. The lungs showed marked hyperemia, serous and hemorrhagic exudation in the alveoli, with partial atelectasis, desquamation of the epithelium of many bronchioles and alveoli, destruction of lymphocytes and phagocytosis in the peribronchial lymphatic tissue, and infiltration of the interlobular septa with large fat or pigment cells and pseudo-eosinophile cells.

Stephens and Florey (1927) attempted to verify the results obtained by Swann (1924), because the death of one of the latter's rabbits, after irradiation for only ten minutes, pointed to some factor independent of roentgen rays. A description of their experiments on blood pressure and on the spleen and heart is given on page 11. They drew attention to the fact that, in Swann's experiments, the unprotected animals had been placed at a distance of from one-half inch to two inches from the tube and that, under these conditions, electrical leakage through the animal from the tube and high tension leads was inevitable, especially with the animal lying on a copper table. This source of error was avoided by means of a suitable electrical screen, and Stephens and Florey did not observe the fall in blood pressure and the cardiac manifestations noted by Swann. To test the effect of roentgen rays on respiration, a rabbit was anesthetized with urethane and then subjected to continuous irradiation[163] for one hour, partly with and partly without the electrical screen; during this time a respiratory tracing was made from a tracheal cannula. The irradiation had no demonstrable effect on respiration, and a repetition of the experiment also yielded a negative result.

Hartman, Bolliger, Doub, and Smith (1927) exposed to roentgen rays[164] the anterior thoracic wall of thirteen dogs and five sheep through a field 7 by 9 cm. and 10 by 12 cm., respectively. Three of the dogs, which had been irradiated for from 75 to 280 minutes, died within thirty days, apparently from causes unrelated to the irradiation. Five of the sheep, which had been exposed to the rays for from 120 to 280 minutes, also died within thirty days, apparently as a direct result of irradiation. The dogs and sheep ate well and most of them remained in a good state of nutrition, but some were abnormally quiet and tended to

[163] Rays generated at a potential equivalent to a spark-gap of 11 cm.; with a current of 1.5 ma., at a focal-skin distance of approximately 15 cm.

[164] The rays were generated by a water-cooled tube operating at 200 kv., filtered through 1 mm. of copper and 1 mm. of aluminium, at a focal-skin distance of 50 cm., with 30 ma. of current. Under these conditions, an exposure of 15 minutes represented one human erythema dose.

lie around in the cages. The remainder of the animals survived three months or longer. In the animals surviving less than thirty days, the skin of the exposed territory usually exhibited depilation and often ulceration also. Passive hyperemia and edema of the thoracic tissues in the field of irradiation were found at necropsy. The skin was abnormally thick and tough. Passive hyperemia of the abdominal organs was constant. The lungs of the sheep, especially the lower lobes, were voluminous, and scattered patches of thickening were visible in the pleura, but effusion did not occur. On section, the lower lobes were almost solid and contained a large quantity of thin, foamy fluid. The pericardial sac of all the sheep contained from 80 to 150 c.c. of fluid, but the pericardium throughout was smooth and glistening The heart was distended from two to three times beyond normal size, and this dilatation affected chiefly the right auricle and ventricle. Microscopic examination of sections from the ventricles and interventricular septum yielded evidence of myocardial degeneration, hyperemia and occasional hemorrhages, moderate infiltration by round and wandering cells and, in one of the sheep which had been irradiated for 240 minutes within thirty days, marked polymorphonuclear infiltration of the cardiac muscle.

Four dogs, which had been irradiated over the anterior thoracic wall for from 130 to 155 minutes in from three to five months, remained in good condition, but two developed late ulceration and cachexia. The cardiac abnormalities found at necropsy were of the same character as, but more marked than, in the animals that died within thirty days. The right auricle always gave evidence of a hemorrhagic process resembling that described by Davis. The valves were always intact. The walls of the blood vessels were thickened or actually obliterated. Hemorrhage and hyaline degeneration were not found in the wall of the right and left ventricles or in the interventricular septum. Instead, atrophy of the muscle fibers, with indistinct striations, and granulation and vacuolization of the cytoplasm were found. Many fibers were replaced by homogeneous, hyaline material. The interstitial tissue was abundant, finely granular or vacuolated, especially around the small blood vessels.

The entire anterior thoracic wall, including the region of the liver, of a second series of eight dogs was irradiated through a field 15 by 15 cm., but the dose given to each animal, the number of exposures, and the interval between the exposures were not specified. An effort was made to exclude the stomach and intestine from the path of the rays. More pronounced fibrosis of lungs and liver were found, but the cardiac alterations resembled those noted in the animals of the first series. The right side of the thorax of the three other animals was exposed to roentgen rays through a field 7 by 9 cm. Two of the animals apparently survived an unspecified dose of radiation, since only one, which had been irradiated for 190 minutes in four months, came to necropsy. This animal, weighing 25 kilograms, remained fairly active and well nourished, but became cyanotic on exertion. The abnormalities noted included: hyperemia of the abdominal organs and kidneys, thickening of the pleura and focal pulmonary fibrosis, moderate hydropericardium with a smooth membrane, a heart weight of 139 grams, roughening and grayish-red color of the lower half of the right ventricle and tip of the left ventricle, grayish-red color of the auricles without thickening or hemorrhage, gray and reddish-brown mottling of the portion of the ventricular walls corresponding to the roughened area of the epicardium, softening of the interventricular septum, thickening and hyaline degeneration of the epicardium, hemorrhage, atrophy, and granular and vacuolar degeneration of the muscle fibers, and degeneration and atrophy of the muscle fibers of the right auricle without hemorrhage. The electrocardiographic abnormalities have been mentioned elsewhere (page 9).

Hartman, Bolliger, Doub, and Smith concluded that sufficient doses of roentgen rays may injure the heart and that irradiation provides a non-surgical, experimental method of inducing myocardial lesions, but they made no deductions with reference to the accompanying abnormalities in the lungs.

Warthin and Pohle (1929) pursued their investigation of the effect of roentgen rays on the heart by exposing the precordial region of forty-eight rats and twenty-four rabbits to an initial dose of 600 R[165] at one session and, at intervals of one month, to two subsequent doses of 300 R each of roentgen rays of moderate and short wave-length. The animals were killed from eight to thirty-two days after the last exposure. Further details are given elsewhere (page 22). All the irradiated animals showed myocardial lesions in the form of hyaline and fatty degeneration and Zenker necrosis, and sometimes of varying degrees of inflammatory reaction and interstitial proliferation. These cardiac changes were complicated by more or less marked catarrhal or purulent bronchitis and bronchopneumonia affecting the large bronchi and the portions of the lungs in the anterior mediastinum. Local or generalized mediastinitis and early pleuritis and pericarditis also were noted, and colonies of bacteria were found in all the lesions. Pulmonary and myocardial lesions of the same character, though not so severe in degree, were also noted in the majority of the unirradiated control animals, and this made it difficult to evaluate the irradiation factor in the myocardial alterations described. Moreover, in addition to pulmonary infection, three of the control rabbits presented myocardial lesions common to "rabbit encephalitis." Because the myocardial and associated pulmonary changes were less pronounced in the control animals, it was felt that the cardiac lesions, at least in large measure, were due to irradiation. Warthin and Pohle concluded that the rays had caused a primary injury to the heart, large bronchi, portions of the lungs, lymph nodes, thymus, and mediastinal ganglions; a secondary, infective bronchitis and bronchopneumonia often extended to the pleura, mediastinum, and pericardium, and the changes incident to such secondary infection usually were more severe in the irradiated than in the unirradiated animals. They considered it probable that the control animals became infected by being kept with the irradiated animals, and that the secondary infection may have extended directly to the pericardium and heart or that the heart may have become involved by hematogenous infection of the endocardium (one animal had shown thrombo-endocarditis).

Lüdin and Werthemann (1930) undertook to investigate the lung changes induced in animals by doses of roentgen rays sufficient to affect the lungs but not so large as to kill the animals before pulmonary alterations should have time to develop. In a first series of experiments, the anterior and posterior aspects of the thorax of five adult rabbits were exposed, through fields 5x5 cm., to 500 r of roentgen rays.[166] The anterior and posterior thoracic fields were irradiated alternately once a week,[167] until the animals died. In every case sections from different parts of the lungs were prepared immediately after death.

The anterior surface of the thorax of one rabbit was irradiated eight times, and the posterior surface nine times, at weekly intervals, in one hundred and thirty-one days (total, 8,500 r). The anterior surface of the thorax of one rabbit was irradiated twelve times, and the posterior surface twelve times, at weekly intervals, in one hundred and eighty-seven days (total, 12,000 r). The anterior surface of the thorax of one rabbit was irradiated eleven times, and the posterior surface twelve times, at weekly intervals, in one hundred and eighty-three days (total, 11,500 r). The anterior surface of the thorax of one rabbit was irradiated thirteen times, and the posterior surface sixteen times, at weekly intervals, in two hundred and forty-one days (total 14,500 r). The anterior surface of the thorax of one rabbit was irradiated twenty-one times, and the posterior surface twenty-two times, at weekly intervals, in three hundred and forty-three days (total, 21,500 r).

In a second series of experiments, the thorax of six adult rabbits was irradiated in the same manner as in the animals of the first series, with the single exception that the size of the anterior and posterior fields was increased to 12x12 cm. The anterior surface of the thorax of one rabbit was irradiated five times, and the posterior surface five times, at inter-

[165] German R.

[166] Rays generated at 160 kv., filtered through 8 mm. of aluminium, at a focal-skin distance of 23 cm.; half-value layer of copper, 0.55 mm.

[167] 500 r per field or per week.

vals of two weeks, in sixty-five days (total, 5,000 r). The anterior surface of the thorax of one rabbit was irradiated seven times, and the posterior surface seven times, at intervals of two weeks, in ninety-eight days (total, 7,000 r). The anterior surface of the thorax of one rabbit was irradiated seven times, and the posterior surface seven times, at intervals of two weeks, in ninety-nine days (7,000 r). The anterior surface of the thorax of one rabbit was irradiated seven times, and the posterior surface eight times, at intervals of two weeks, in one hundred days (total, 7,500 r). The anterior surface of the thorax of one rabbit was irradiated seven times, and the posterior surface seven times, at intervals of two weeks, in ninety-eight days (total, 7,000 r). The anterior surface of the thorax of one rabbit was irradiated eight times, and the posterior surface seven times, at intervals of two weeks, in one hundred and twenty-seven days (total, 7,500 r).

The affected parts of the lungs could be readily perceived, even with the naked eye. In only two rabbits did the pleural cavity contain fibrinous exudate and the lungs adhere to the parietal pleura. The affected lobes were pale and their consistency increased. The cut surface was gray and displayed definite pneumonic granulation. The lumen of the bronchi contained yellowish white, sticky, purulent exudate, but smears did not show any microorganisms. In areas not diffusely infiltrated by pneumonia, dark red or yellowish spots were interspersed with areas of greater consistency.

When examined microscopically, even the lobes which superficially appeared normal presented scattered areas that did not contain air. Some of the interalveolar septa were abnormally thick, and the capillaries were gorged with leucocytes. Adjacent groups of alveoli contained masses of exudate. In other areas emphysema had torn the alveolar septa, the alveolar epithelium was sometimes lacking, and elastic fibers were knotted together. Even in the lobes where the pathologic changes were least pronounced, desquamation of the bronchial epithelium and increased secretion of mucus were noted. The marked sclerosis of the vessels, found in some cases, was not regarded as an effect of irradiation, because similar sclerosis was found in the lungs of unirradiated, control animals. The alveolar epithelium sometimes showed vacuolar degeneration of the protoplasm and occasional swelling or disappearance of the nuclei, and some of the cells had desquamated. In the bronchioles, however, the epithelium had become cuboidal, multinucleated giant-cells had formed, and mitotic division had increased. In some of the interalveolar septa the capillaries were greatly distended with cells. Some of the lungs showed marked purulent bronchitis, bronchiolitis, and bronchopneumonia. Groups of alveoli related to certain bronchi did not contain air and were filled with leucocytes, cellular débris, and mucus. Here and there abundant deposits of fibrin were visible. The larger bronchi, some of which were filled with pus, and sometimes the blood vessels also, were surrounded by inflammatory infiltration. In some of the lungs severe bronchopneumonia was apparent; sometimes entire lobes were involved. In such areas the alveolar epithelium had undergone marked degeneration and desquamation.

In the animals of the second series the pulmonary changes were more extensive, and involvement of entire lobes was more frequent. More or less pronounced proliferation of the bronchial epithelium, which had been observed in only a few animals of the first series, was found in all the animals of the second series. Often the several layers of cells were infiltrated with leucocytes. Still more striking was the cellular proliferation around the pneumonic areas of peribronchial tissue; this had the bud-like characteristics of epithelial regeneration, undoubtedly to replace the injured epithelium of the aveoli. Such regenerative features were always associated with severe bronchopneumonic inflammation, but many sections showed it around the original alveoli, the epithelium of which had degenerated and been destroyed. In some sections, epithelial proliferation was so extensive as almost to suggest carcinoma. In the heart, pathologic changes including cloudy swelling of the myocardium, with fading or disappearance of cross striations, waxy degeneration of muscle fibers, vacuolar degeneration and finely granular appearance of the sarcoplasm, swelling and de-

generation of the longitudinal fibrils, absence of fatty degeneration, atrophy and disappearance of some of the fibers, diminution in the number of nuclei in the areas of degeneration, slight or marked perivascular inflammatory infiltration, and sometimes interstitial connective tissue sclerosis were found.

Lüdin and Werthemann summed up their results as follows: In all the animals that died a circumscribed bronchopneumonia was found as the initial pulmonary change; later the pneumonic areas coalesced, and the inflammatory process was accompanied by marked purulent bronchitis. Swelling, vacuolar degeneration of the protoplasm, disappearance of nuclei, and cellular disintegration of the alveolar epithelium occurred. The bronchopneumonic foci were surrounded by pronounced edema and desquamative catarrh. The bronchial epithelium showed a strong tendency to proliferate, and the layers of epithelial cells in the bronchial mucosa increased in number. Regenerative epithelial proliferation was evident also in the alveoli. Numerous atypical mitotic figures, polymorphism of cells, and nuclear pycnosis and disintegration featured the proliferative changes.

Radium. Pappenheim and Plesch (1913) investigated the effect of thorium X on the body by introducing this radioactive substance, intravenously or by mouth, into six rabbits. The blood was examined microscopically twice a day, and the bone marrow of the femur, tibia, humerus, and radius was examined six, twenty-four, and forty-eight hours, and three days after administration of thorium. The parenchymatous organs, bone marrow, and sometimes the inguinal and mesenteric lymph nodes, were fixed while still warm by the method of Orth and Helly, and sections were stained by the combined May-Giemsa acetic acid method. The testis was fixed in a mixture of Orth 5 and Hermann 1 and stained with methyl green-pyronin and with Pappenheim's panchrom picrin.

The first rabbit was killed four days after the intravenous injection of three million Mache units of thorium X. Before death, the blood showed an increasing leucopenia affecting chiefly the lymphocytes and large mononuclear cells, and at necropsy a scanty, fluid bone marrow the color of mulberry jelly was found to consist largely of anuclear erythrocytes, with a few basophilic normoblasts, lymphoidocytes, megacaryocytes, promyelocytes, irritation cells, but no orthochromatic erythroblasts or myelocytes. This was accompanied by marked hyperemia and hemorrhages in the alveolar spaces. The second rabbit, which died three days after an intravenous injection of four million Mache units of thorium X, also presented a marked reduction in the number of leucocytes, especially of lymphocytes, and blood platelets; an increasing hyperemia of the bone marrow, with free hemorrhage and great destruction of cells; hyperemia, proliferative thickening of the trabecular connective tissue and walls of the blood vessels; marked destruction of lymphocytes, atrophy of the follicles, and hemorrhages in the spleen; extreme, central, vascular, congestive dilatation and hemorrhage, and central necrosis of the parenchyma of the liver; hyperemia of the kidneys, with exudative distention of the capsules of the glomeruli and coagulation necrosis; moderate congestion and slight necrosis of the suprarenals; and intense hyperemia of the lungs with extreme distention of the interalveolar capillaries. Similar changes were found in the fourth rabbit, which had received intravenously five million Mache units of thorium X on each of two occasions, with an interval of two days, and died two days after the second injection.

The fifth rabbit was given nine million Mache units of thorium X in water, through a stomach tube, to ascertain if absorption from the intestine might cause greater periportal changes in the liver. The animal died three days later, and the alterations in the liver, kidneys, spleen, and bone marrow, closely resembled those found in the previous animals. In addition to the extensive destruction of lymphocytes in the spleen and lymph nodes, a greenish pigment was deposited widely in these structures, between the villi of the intestine and in the gastric glands. The lungs also showed hyperemia, exudative dilatation of the alveoli, and brownish pigment scattered in the alveolar epithelium. The sixth rabbit, which received intravenously seven and one-half million Mache units and, four days later, twelve

million Mache units of thorium X, died two days after the second injection. The abnormalities found in this animal were the same as those noted in the others.

Pappenheim and Plesch thought the changes affecting the lymphoid cells of the follicles of the spleen and lymph nodes represented atrophy of these cells, some of which were described as having been transformed into connective tissue cells. Hyperemia and proliferation of connective tissue cells between the follicles and in the trabeculae also were regarded as factors in the atrophy of the lymphoid elements. They called attention to the fact that the liver sustained the greatest injury from intravenous injection of thorium X, while oral administration injured the kidney more than other internal structures, exclusive of the blood-forming organs. They were led to the conclusion that the first effect of thorium X was to injure the endothelium of the vessel walls and then to cause a direct toxic effect on the parenchymatous cells of the bone marrow, lung, liver, kidney, spleen, and lymph nodes.

Lazarus-Barlow (1922) exposed the entire body of twenty frogs, twenty-eight rats, fifteen rabbits, and nine cats to the gamma rays emitted by 5 grams of radium. A description of these experiments is given elsewhere (page 34). No clinical disturbances of any kind were noted in the majority of the animals, but the rabbits that survived, after exposure for forty-eight hours, became somnolent, and, in one instance, hemorrhage from the ears occurred. Loss of weight was noted in six out of seven animals; in two an initial loss of weight was made up during the second week after exposure. There was no evidence of diarrhea, but after prolonged exposure the function of the intestine was impaired. In the cats symptoms did not appear for one or two days after exposure, but soon or long after this, according to the duration of exposure, the animals refused food and became somnolent; mucus sometimes exuded from the mouth or anus, and diarrhea occurred in some cases. After short exposures, the gastrointestinal tract was distended by liquid contents. The spleen was always abnormally small. After prolonged exposures, petechial or more extensive hemorrhages were found in the mucous membrane of the stomach, intestine, bladder, muscles, lymph nodes, sex glands, and bone marrow. The gastrointestinal tract was greatly distended and contained large amounts of mucus often mixed with blood. Extensive degeneration of leucocytes, especially lymphocytes, was observed in the circulating blood, spleen, lymph nodes, intestinal lymph follicles, and bone marrow; pronounced degenerative changes were also found in the testis or ovary, stomach and intestine, kidneys, liver, and other organs. The striation of the cardiac muscle fibers was not affected by short exposures, but became less and less distinct as the duration of exposure increased. The contractile material in the myocardium became finely granular and fibrillar, hyaline or translucent, or vacuolated and fragmented, as the irradiation or the period of survival was prolonged.

So far as the lungs were concerned, even short exposures were followed by congestion, exudation, and alteration of the columnar epithelium lining the air-passages. These changes were greatest in the cat and least in the rabbit. After short exposures, the capillaries were widely dilated, and a few erythrocytes or granular débris were found in the alveolar spaces. Small patches of collapse or consolidation alternating with emphysema were sometimes noted; after longer exposure or survival, the consolidation recalled lobar pneumonia in man, but this was patchy and free from polymorphonuclear leucocytes. The nuclei of the endothelial cells lining the alveoli were usually vesicular and faintly stained, but, after prolonged exposure, they were irregularly contracted and deeply stained. Desquamation of alveolar epithelium was always slight. The columnar epithelium of the bronchi and trachea usually showed degeneration and desquamation, sometimes associated with proliferation. The formation of mucus, through goblet cells and mucoid degeneration of the columnar epithelium, was the most salient modification. In the rabbit free mucus was not found in the air passages, but the cells were swollen and ready to desquamate. Mucoid degeneration was moderate in the rat and frog and intense in the cat. The submucous tissue and its mucous glands were "swollen bags of mucus." The peribronchial lymphoid tissue was remarkable for the absence of lymphocytes, the presence of nuclear débris, and the prominence of endothelial cells.

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To be Continued.